Hybrid ablation of atrial fibrillation

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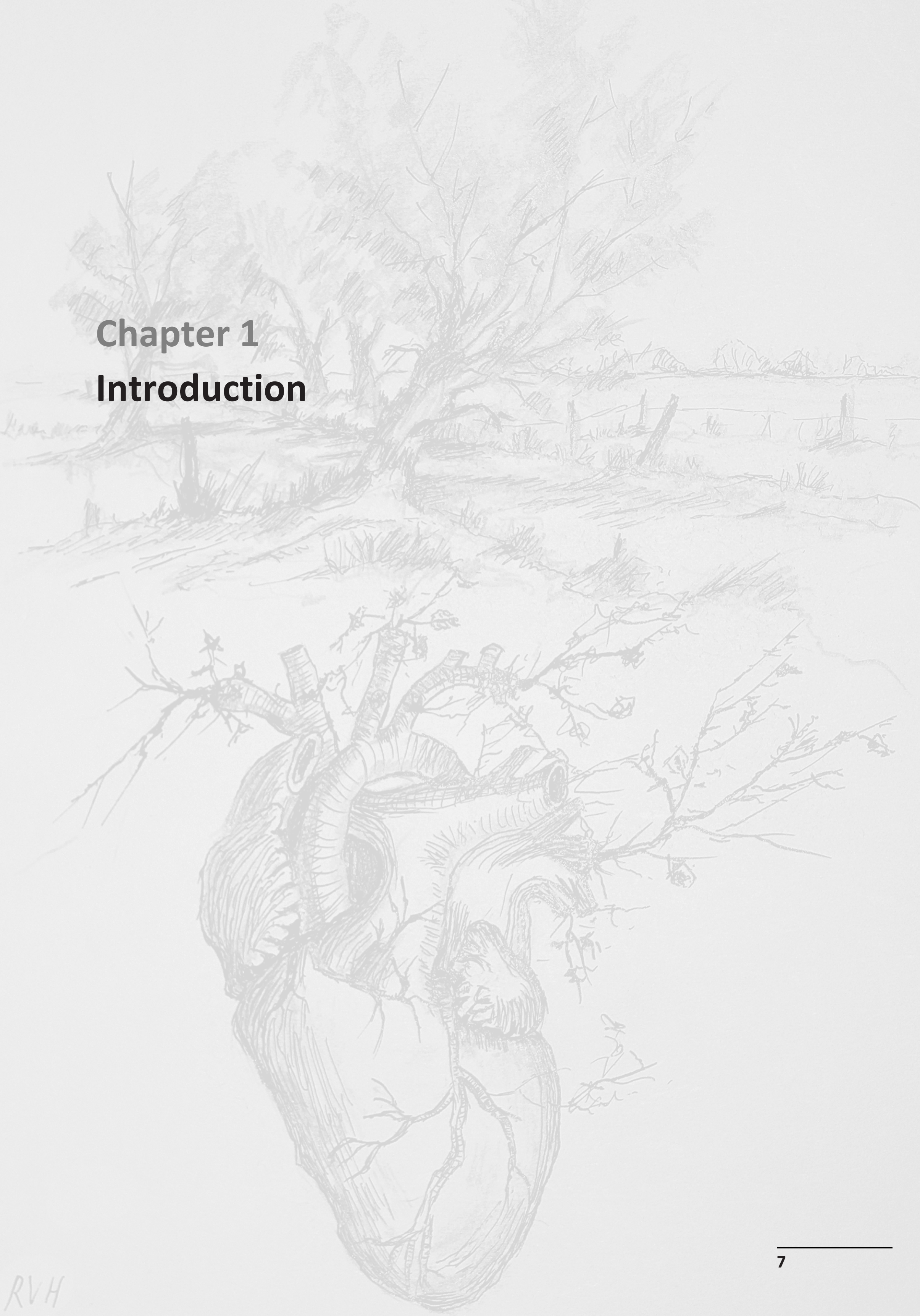
Chapter 1
Introduction



A. Setting the stage: atrial fibrillation is an increasing public health challenge

Atrial fibrillation (AF) is the most common cardiac arrhythmia with an incidence that remains relatively low until around the seventh decade and from then on exponentially increases.[1] The reported prevalence in the general population was around 1% to 2% at the end of the 20th century, ranging from 0.1% of adults aged less than 55 years to at least 10% of octogenarians.[2, 3] Heeringa et al. showed that the life-time risk of developing AF in adults aged 55 years or more, was 23.8% in men and 22.2% in women.[4] The life-time risk of developing AF in adults aged 40 years or more, was one in four in the Framingham Heart Study.[5] AF has been shown to be an independent predictor of cardiovascular and all-cause mortality.[6-10] Epidemiological and clinical studies have also proven that AF is a strong independent risk factor for stroke, exposing patients to a 3- to 5-fold increased risk.[11] Uncontrolled AF may contribute to the development of chronic heart failure.[6, 12, 13] The overall economic burden of AF in 2006 ranged from €526 million in Poland to €3286 million in Italy, with the largest proportion of direct costs related to hospitalizations.[14-19] Due to the increasing age of the general population, the AF burden will grow further. By the year 2050, there will be a 2.5-fold increase in the number of affected US adults, resulting in almost 6 million patients and half of them will be 80 years or older.[2]

B. AF management

The goals of AF management are the reduction of symptoms and the prevention of complications associated with this arrhythmia. The latter relies on antithrombotic therapy, control of ventricular rate, and therapy of concomitant cardiac diseases. These therapeutic interventions may suffice to achieve the former goal but a substantial number of patients will need additional rhythm control therapy to relieve symptoms. Additional rhythm control can be achieved by cardioversion, antiarrhythmic drug (AAD) therapy, or ablation therapy.

The cornerstone of endocardial catheter ablation procedures for AF is ablation of the ostium or antrum of the pulmonary veins (PV) with the endpoint of electrical isolation of these veins from the left atrium (LA). The rationale for this, is the seminal observation by Haissaguerre et al. in 1998 that AF was almost always triggered by ectopic beats arising from the muscle sleeves of the PVs.[20] The success rate of PV isolation in patients with paroxysmal AF, is greater than 80% and the most frequent reason for AF recurrence is PV reconduction.[21, 22] However, long-term results of catheter ablation for paroxysmal AF are less satisfying: in a recently published prospective study, sinus rhythm was maintained in 46% of patients after the initial procedure without AAD during a median follow-up period of 5 years.[23]

In patients with persistent or longstanding persistent AF, PV isolation alone results in success rates below 25%.[24] This is likely due to the fact that as AF progresses from paroxysmal to persistent, the atrial substrate itself may play a relatively more important role in AF maintenance.[25] Ablation of the atria is called "substrate modification" and consists of linear lesions and/or ablation of complex fractionated atrial electrograms (CFAE). The creation of linear lesions was inspired by the surgical Cox-maze procedure for AF.[26] However, the creation of these linear lesions endocardially can be challenging and incomplete lesions may become themselves proarrhythmic and result in macro-re-entrant circuits.[27] Catheter ablation procedures using PV isolation in combination with linear lesions and/or CFAE ablation in patients with persistent and longstanding persistent AF, seem to result in a better outcome than PV isolation alone but there is an important variation is success rates going from 11 to 75% and the incidence of ATs after this kind of procedures goes up to 40%.[28, 29] There seems to be a slow but steady decline in arrhythmia-free survival, especially after catheter ablation for persistent AF.[30]

Dr. James Cox performed the first successful surgical treatment of AF in 1987.[31, 32] At that time, the procedure involved the creation of several incisions in both atria. These linear lesions were thought to prevent sustained multiple re-entry circuits by compartmentalization of the atria and to direct the sinus node impulse through the atrial tissue. This procedure is known as the Cox-maze III procedure or "cut-and-sew" maze and became the gold standard for the surgical treatment of AF. Although resulting in more than 95% of freedom from symptomatic AF at a mean follow-up of 5 years, this procedure didn't gain widespread implementation due to its complexity and surgical challenge.[33] To render this procedure less intimidating for cardiac surgeons, new technologies were introduced to replace the incisions of the Cox-maze III with linear lines of ablation.[34, 35] By performing these linear lesions with bipolar radiofrequency ablation, Damiano et al. introduced the Cox-maze IV procedure.[36] This procedure still requires cardiopulmonary bypass. Several new ablation technologies have been introduced over the last decade with the ultimate goal to perform a complete lesion set epicardially on the beating heart, without the need for cardiopulmonary bypass. The Achilles heel of many of these energy sources, however, is their inability to guarantee reliable transmural lesions on the beating heart.[35, 37]

C. Aims and outline of this thesis

In this thesis, we hypothesized that a hybrid or convergent AF ablation procedure is feasible and safe and, by integrating the best aspects of endocardial transcatheter and epicardial off-pump surgical techniques, has the potential to result in improved success rates. The surgeon is able to perform PV isolation epicardially, deploy a number of linear ablation lines and exclude the left atrial appendage (LAA). The electrophysiologist can realize endocardial validation of those epicardial lesions, perform endocardial (touch-up) ablation where necessary and target atrial tachycardias or flutters that may occur during the procedure.

Chapter 2 summarizes the findings of the EHRA EP Wire survey on currently used endocardial AF ablation techniques, with the emphasis on different lesion sets, energy sources and imaging modalities.

In chapter 3, we provided an overview of minimal invasive surgical AF ablation techniques. Current procedures are building on knowledge derived from the Cox-maze III procedure but try to be less invasive. We described the technical aspects of these procedures and their outcome.

In chapter 4, we summarized the results of the EHRA EP Wire survey on surgical and hybrid AF ablation procedures. The purpose of this online questionnaire, was to survey clinical practice in European centres as the variety of surgical techniques and the heterogeneity of treated patients make the comparison of results and outcomes challenging.

Chapter 5 puts 'theory into practice'. We outlined our initial experience with the hybrid thoracoscopic surgical and transvenous catheter ablation approach of AF, focusing on feasibility, safety, and clinical outcomes up to 1 year. To better understand the robustness of the lesion set, we investigated in chapter 6 the safety and feasibility of adenosine administration during hybrid atrial fibrillation ablation to test the occurrence of dormant pulmonary vein conduction.

In chapter 7 we described the occurrence of transient clamp-induced mechanical block of pulmonary vein potentials and the potential clinical implications of this finding.

We highlighted the importance of completely transmural linear lesions in chapter 8 by describing a case of left atrial flutter due to an incomplete left fibrous trigone linear lesion.

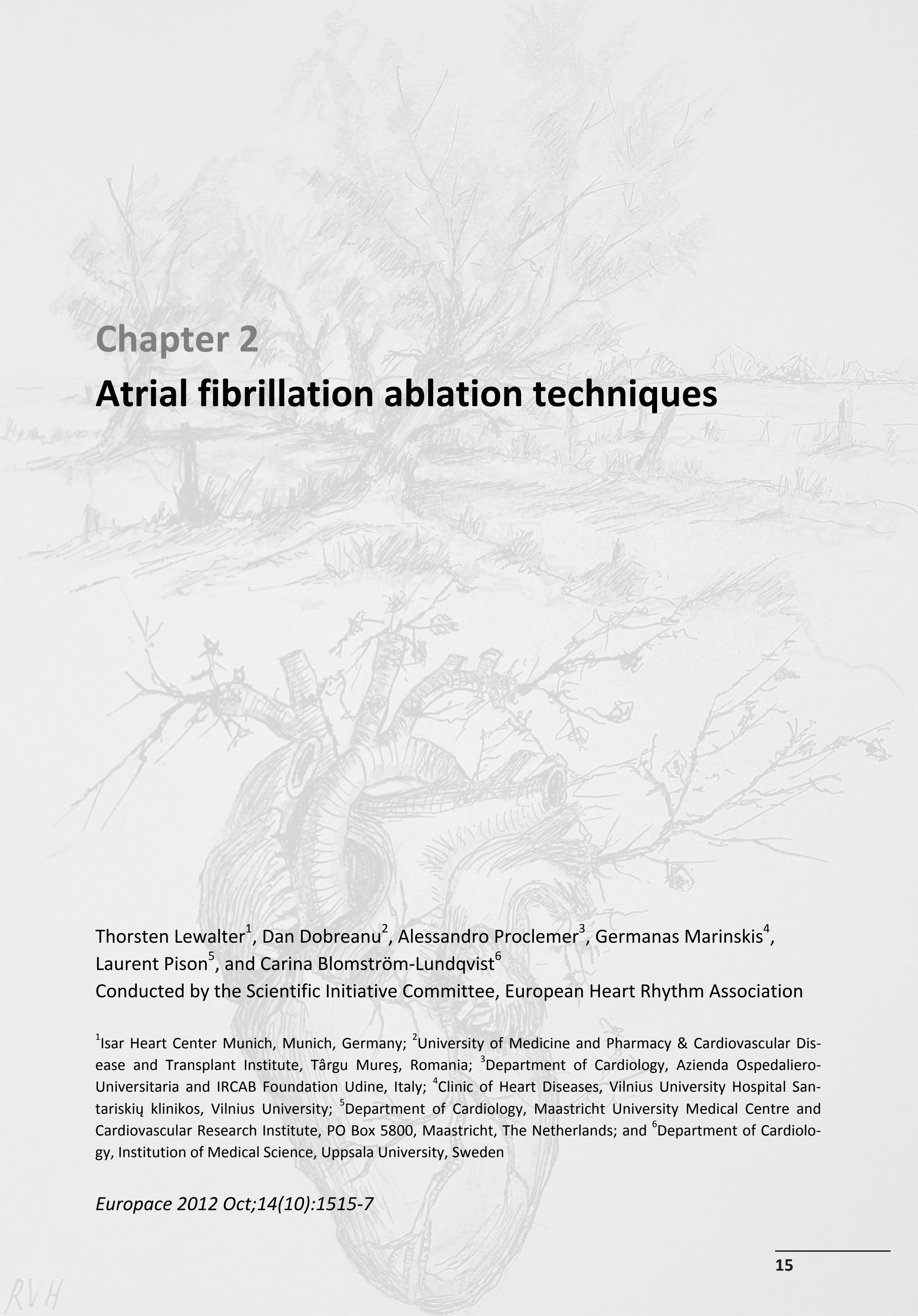
Chapter 9 focuses on the long-term outcome of the hybrid procedure for AF as described in chapter 5.

We briefly reviewed the basic pathophysiological aspects of AF which guide the invasive treatment of this arrhythmia in chapter 10. The strengths and weaknesses of both the transvenous catheter and epicardial surgical ablation approach were highlighted. We explained the rationale for a hybrid or convergent procedure and, finally, focused on current challenges and future developments.

References

1. Wolf PA, Benjamin EJ, Belanger AJ, Kannel WB, Levy D, D'Agostino RB. Secular trends in the prevalence of atrial fibrillation: The framingham study. *American heart journal*. 1996;131:790-795
2. Go AS, Hylek EM, Phillips KA, Chang Y, Henault LE, Selby JV, Singer DE. Prevalence of diagnosed atrial fibrillation in adults: National implications for rhythm management and stroke prevention: The anticoagulation and risk factors in atrial fibrillation (atria) study. *JAMA : the journal of the American Medical Association*. 2001;285:2370-2375
3. Feinberg WM, Blackshear JL, Laupacis A, Kronmal R, Hart RG. Prevalence, age distribution, and gender of patients with atrial fibrillation. Analysis and implications. *Archives of internal medicine*. 1995;155:469-473
4. Heeringa J, van der Kuip DA, Hofman A, Kors JA, van Herpen G, Stricker BH, Stijnen T, Lip GY, Witteman JC. Prevalence, incidence and lifetime risk of atrial fibrillation: The rotterdam study. *European heart journal*. 2006;27:949-953
5. Lloyd-Jones DM, Wang TJ, Leip EP, Larson MG, Levy D, Vasan RS, D'Agostino RB, Massaro JM, Beiser A, Wolf PA, Benjamin EJ. Lifetime risk for development of atrial fibrillation: The framingham heart study. *Circulation*. 2004;110:1042-1046
6. Stewart S, Hart CL, Hole DJ, McMurray JJ. A population-based study of the long-term risks associated with atrial fibrillation: 20-year follow-up of the renfrew/paisley study. *The American journal of medicine*. 2002;113:359-364
7. Stewart S, MacIntyre K, MacLeod MM, Bailey AE, Capewell S, McMurray JJ. Trends in hospital activity, morbidity and case fatality related to atrial fibrillation in scotland, 1986--1996. *European heart journal*. 2001;22:693-701
8. Wattigney WA, Mensah GA, Croft JB. Increasing trends in hospitalization for atrial fibrillation in the united states, 1985 through 1999: Implications for primary prevention. *Circulation*. 2003;108:711-716
9. Benjamin EJ, Wolf PA, D'Agostino RB, Silbershatz H, Kannel WB, Levy D. Impact of atrial fibrillation on the risk of death: The framingham heart study. *Circulation*. 1998;98:946-952
10. Wolf PA, Mitchell JB, Baker CS, Kannel WB, D'Agostino RB. Impact of atrial fibrillation on mortality, stroke, and medical costs. *Archives of internal medicine*. 1998;158:229-234
11. Wolf PA, Abbott RD, Kannel WB. Atrial fibrillation as an independent risk factor for stroke: The framingham study. *Stroke; a journal of cerebral circulation*. 1991;22:983-988
12. Shinbane JS, Wood MA, Jensen DN, Ellenbogen KA, Fitzpatrick AP, Scheinman MM. Tachycardia-induced cardiomyopathy: A review of animal models and clinical studies. *Journal of the American College of Cardiology*. 1997;29:709-715
13. Redfield MM, Kay GN, Jenkins LS, Mianulli M, Jensen DN, Ellenbogen KA. Tachycardia-related cardiomyopathy: A common cause of ventricular dysfunction in patients with atrial fibrillation referred for atrioventricular ablation. *Mayo Clinic proceedings. Mayo Clinic*. 2000;75:790-795
14. Le Heuzey JY, Paziaud O, Piot O, Said MA, Copie X, Lavergne T, Guize L. Cost of care distribution in atrial fibrillation patients: The cocaf study. *American heart journal*. 2004;147:121-126
15. Stewart S, Murphy NF, Walker A, McGuire A, McMurray JJ. Cost of an emerging epidemic: An economic analysis of atrial fibrillation in the uk. *Heart*. 2004;90:286-292
16. Coyne KS, Paramore C, Grandy S, Mercader M, Reynolds M, Zimetbaum P. Assessing the direct costs of treating nonvalvular atrial fibrillation in the united states. *Value in health : the journal of the International Society for Pharmacoeconomics and Outcomes Research*. 2006;9:348-356
17. Ringborg A, Nieuwlaat R, Lindgren P, Jonsson B, Fidan D, Maggioni AP, Lopez-Sendon J, Stepinska J, Cokkinos DV, Crijns HJ. Costs of atrial fibrillation in five european countries: Results from the euro heart survey on atrial fibrillation. *Europace : European pacing, arrhythmias, and cardiac electrophysiology : journal of the working groups on cardiac pacing, arrhythmias, and cardiac cellular electrophysiology of the European Society of Cardiology*. 2008;10:403-411

18. McBride D, Mattenklotz AM, Willich SN, Bruggenjurgen B. The costs of care in atrial fibrillation and the effect of treatment modalities in germany. *Value in health : the journal of the International Society for Pharmacoeconomics and Outcomes Research*. 2009;12:293-301
19. Naccarelli GV, Johnston SS, Dalal M, Lin J, Patel PP. Rates and implications for hospitalization of patients ≥65 years of age with atrial fibrillation/flutter. *The American journal of cardiology*. 2012;109:543-549
20. Haissaguerre M, Jais P, Shah DC, Takahashi A, Hocini M, Quiniou G, Garrigue S, Le Mouroux A, Le Metayer P, Clementy J. Spontaneous initiation of atrial fibrillation by ectopic beats originating in the pulmonary veins. *The New England journal of medicine*. 1998;339:659-666
21. Callans DJ, Gerstenfeld EP, Dixit S, Zado E, Vanderhoff M, Ren JF, Marchlinski FE. Efficacy of repeat pulmonary vein isolation procedures in patients with recurrent atrial fibrillation. *Journal of cardiovascular electrophysiology*. 2004;15:1050-1055
22. Thomas SP, Sanders P. Catheter ablation for atrial fibrillation. *Heart, lung & circulation*.21:395-401
23. Ouyang F, Tilz R, Chun J, Schmidt B, Wissner E, Zerm T, Neven K, Kokturk B, Konstantinidou M, Metzner A, Fuernkranz A, Kuck KH. Long-term results of catheter ablation in paroxysmal atrial fibrillation: Lessons from a 5-year follow-up. *Circulation*.122:2368-2377
24. Oral H, Knight BP, Tada H, Ozaydin M, Chugh A, Hassan S, Scharf C, Lai SW, Greenstein R, Pelosi F, Jr., Strickberger SA, Morady F. Pulmonary vein isolation for paroxysmal and persistent atrial fibrillation. *Circulation*. 2002;105:1077-1081
25. Katritsis D, Merchant FM, Mela T, Singh JP, Heist EK, Armoundas AA. Catheter ablation of atrial fibrillation the search for substrate-driven end points. *Journal of the American College of Cardiology*.55:2293-2298
26. Shen J, Bailey M, Damiano RJ, Jr. Surgery for lone atrial fibrillation: Present state-of-the-art. *Innovations (Philadelphia, Pa*. 2009;4:248-255
27. Jais P, Hocini M, O'Neill MD, Klein GJ, Knecht S, Sheiiro M, Arentes L, Kodali S, Clementy J, Haissaguerre M. How to perform linear lesions. *Heart Rhythm*. 2007;4:803-809
28. Rostock T, Drewitz I, Steven D, Hoffmann BA, Salukhe TV, Bock K, Servatius H, Aydin MA, Meinertz T, Willems S. Characterization, mapping, and catheter ablation of recurrent atrial tachycardias after stepwise ablation of long-lasting persistent atrial fibrillation. *Circulation*.3:160-169
29. Brooks AG, Stiles MK, Laborderie J, Lau DH, Kuklik P, Shipp NJ, Hsu LF, Sanders P. Outcomes of long-standing persistent atrial fibrillation ablation: A systematic review. *Heart Rhythm*.7:835-846
30. Weerasooriya R, Khairy P, Litalien J, Macle L, Hocini M, Sacher F, Lellouche N, Knecht S, Wright M, Nault I, Miyazaki S, Scavee C, Clementy J, Haissaguerre M, Jais P. Catheter ablation for atrial fibrillation: Are results maintained at 5 years of follow-up? *Journal of the American College of Cardiology*.57:160-166
31. Cox JL. The surgical treatment of atrial fibrillation. Iv. Surgical technique. *The Journal of thoracic and cardiovascular surgery*. 1991;101:584-592
32. Cox JL, Canavan TE, Schuessler RB, Cain ME, Lindsay BD, Stone C, Smith PK, Corr PB, Boineau JP. The surgical treatment of atrial fibrillation. Ii. Intraoperative electrophysiologic mapping and description of the electrophysiologic basis of atrial flutter and atrial fibrillation. *The Journal of thoracic and cardiovascular surgery*. 1991;101:406-426
33. McCarthy PM, Gillinov AM, Castle L, Chung M, Cosgrove D, 3rd. The cox-maze procedure: The cleveland clinic experience. *Seminars in thoracic and cardiovascular surgery*. 2000;12:25-29
34. Khargi K, Hutten BA, Lemke B, Deneke T. Surgical treatment of atrial fibrillation; a systematic review. *European journal of cardio-thoracic surgery : official journal of the European Association for Cardio-thoracic Surgery*. 2005;27:258-265
35. Damiano RJ, Jr. Alternative energy sources for atrial ablation: Judging the new technology. *The Annals of thoracic surgery*. 2003;75:329-330
36. Lall SC, Melby SJ, Voeller RK, Zierer A, Bailey MS, Guthrie TJ, Moon MR, Moazami N, Lawton JS, Damiano RJ, Jr. The effect of ablation technology on surgical outcomes after the cox-maze procedure: A propensity analysis. *The Journal of thoracic and cardiovascular surgery*. 2007;133:389-396
37. Damiano RJ, Jr., Schuessler RB, Voeller RK. Surgical treatment of atrial fibrillation: A look into the future. *Seminars in thoracic and cardiovascular surgery*. 2007;19:39-45



Chapter 2
Atrial fibrillation ablation techniques

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Conducted by the Scientific Initiative Committee, European Heart Rhythm Association

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Abstract

We performed a survey on current atrial fibrillation (AF) ablation techniques used for catheter ablation of AF among the European Heart Rhythm Association Research Network. The focus of this questionnaire is on the ablation strategy, such as the use of different lesion sets or sites of ablation in the various forms of AF, and on the technical aspects of catheter ablation with respect to energy sources and imaging modalities.

Aims

As a result of limited antiarrhythmic drug efficacy and favourable results in catheter ablation, atrial fibrillation (AF) ablation is becoming more and more established in the field of AF treatment.[1,2] Atrial fibrillation ablation techniques and procedural strategies are on the one hand somehow standardized, like pulmonary vein isolation (PVI) as the desired endpoint in ablating paroxysmal AF,[1,3] on the other hand, clinical everyday practice is characterized by areas of large variations, respectively, among operators. To document the degree of standardization or variation in catheter ablation of AF in clinical routine, we performed the herewith presented survey.

Methods and results

Responses were received from 46 partners of the European Heart Rhythm Association Research Network, with the majority of centres being university hospitals (67.4%).

With respect to the pattern of AF in patients who undergo ablation in these centres, 33 or 82.5% of centres indicate that paroxysmal AF counts for >50% of their ablation indication. In 28 or 74% of the centres, persistent AF with a duration of <1 year exhibits 10–30% of their ablation indication. The vast majority (33 centres or 91.7%) estimate long-standing persistent AF as a minor ablation indication (<10% of ablated patients). Twenty-one centres or 54% do not perform AF ablation as a first-line therapy, whereas in 18% of the centres first-line therapy in drug-naïve patients is already forming a group of 10–20% in their ablation cohort.

Atrial fibrillation ablation, mapping, and imaging equipment

Regarding ablation and imaging equipment, 24 centres (63%) are using a Carto or NavX system in more than 70% of their ablation cases, whereas rotational angiography, intracardiac echocardiography, the Hansen Robotic System, and Magnetic Navigation systems are only used in a minority of cases and centres. As expected, radiofrequency is the most frequently used energy source (15 centres use it in >70% of all cases), but cryoenergy is also used by 5 or 21% of centres in more than 70% of their AF ablations. Laser light is so far used only by two centres in 10–30% of AF ablation. Oesophageal temperature monitoring is not performed by 23 centres or 59% because they believe, that this method is not necessary of helpful at all, whereas three centres (8%) use it for all cases, two centres (5%) only for radiofrequency ablations, and seven centres (18%) only in selected cases such as lines in the posterior wall. Four centres (10.3%) do not use oesophageal temperature monitoring because they only use cryoenergy and they believe that for this energy source temperature monitoring does not make sense.

Ablation strategy, success rate, and follow-up in paroxysmal atrial fibrillation

The vast majority of centres (32 or 82%) perform PVI as the preferred strategy in paroxysmal AF. Five centres (13%) do a priori PVI + lines or complex fractionated atrial electrogram (CFAE)-ablation as their primary ablation strategy. Looking specifically into catheter designs used for paroxysmal AF ablation, cooled tip ablation (in more than 70% of cases in 21 centres/62%) and the cryo-balloon [seven centres (32%) use it in more than 70% of their cases] are the most frequently used catheter designs (for details see Table 1). The estimated ablation success (defined as percentage of patients free from symptomatic AF without antiarrhythmic drugs) after the first ablation procedure within 1 year is close to the published data: 18 centres (47%) indicate an ablation success as defined above 60–70% of their cases. Thirty-seven percent or 14 centres estimate their success in the 50–60% range; only one centre has a success rate of >70% and two centres state an ablation success rate of <40%. To assess recurrence of paroxysmal AF episodes, nearly all centres use clinical evaluation (91%), resting electrocardiogram (ECG) (88%) and 24-h Holter (79%). More than 50% of all centres use stress ECG, 7-day Holter, yet external or implantable loop recorders only in <10% of their cases as a follow-up tool.

Table 1. Which catheter design do you use for paroxysmal atrial fibrillation ablation?

	<10%	10 – 30%	30 – 50%	50 – 70%	>70%	Response count
Cooled tip (= irrigated)	2.9% (1)	11.8% (4)	8.8% (3)	14.7% (5)	61.8% (21)	34
Solid tip (4 mm)	85.7% (6)	14.3% (1)	0.0% (0)	0.0% (0)	0.0% (0)	7
Solid tip (8 mm)	55.6% (5)	11.1% (1)	11.1% (1)	11.1% (1)	11.1% (1)	9
Cryo-balloon	27.3% (6)	22.7% (5)	13.6% (3)	4.5% (1)	31.8% (7)	22
Laser-balloon	75.0% (6)	25.0% (2)	0.0% (0)	0.0% (0)	0.0% (0)	8
Circular RF ablation catheter	64.3% (9)	7.1% (1)	21.4% (3)	7.1% (1)	0.0% (0)	14
Other	100.0% (9)	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	9

RF, radiofrequency.

Ablation strategy, success rate, and follow-up in persistent atrial fibrillation

Interestingly, 17 centres (45%) perform AF ablation in persistent but not in long-standing persistent AF, whereas 19 centres (50%) perform ablation also in long-standing persistent AF. In persistent AF with <1 year of duration, PVI is the primary ablation strategy in 13 centres or 37.1%, whereas seven centres perform PVI + CFAE ablation and six centres PVI + left atrial lines and nine centres PVI + lines + CFAE ablation as the primary and first ablation strategy. In long-standing persistent AF with an AF duration of >1 year, 14 centres (47%) use the complete approach with PVI + lines + CFAE ablation as their primary strategy, whereas three centres (10%) use only PVI for the first procedure. For all forms of persistent AF ablation, using a three-dimensional (3D) guiding system with either the NavX (13 centres/37%) or the CARTO system (20 centres/57%) is the standard of care. Regarding the estimated rate of success for all forms of persistent AF including multiple procedures, success rate I (=asymptomatic, AF free without antiarrhythmic drugs) is most frequently seen between 40 and 50%, whereas success rate II (with antiarrhythmic drugs) is at a level of 60–70% in the majority of centres (see details in Table 2, especially the distribution of estimated success rate without antiarrhythmic drugs with 10 centres <40% and 10 centres >50%).

Twenty-three centres (64%) experience recurrent atrial tachycardias at a rate of 5–15% following their ablation procedures, five centres observe this in more than 15% of their cases, and three centres see atrial regular tachycardias in >25% after ablation of persistent AF.

Table 2. How do you estimate your success rate (Success-I=asymptomatic patients, AF free without antiarrhythmic drugs. Success-II=asymptomatic patients, AF free including those with antiarrhythmic drugs) for all forms of persistent AF including multiple procedures?

	<40%	40 – 50%	50 – 60%	60 – 70%	>70%	Response count
Success-I (without antiarrhythmic drugs)	29.4% (10)	35.3% (12)	29.4% (10)	5.9% (2)	0.0% (0)	34
Success-II (with antiarrhythmic drugs)	2.8% (1)	22.2% (8)	30.6% (11)	36.1% (13)	8.3% (3)	36

AF, atrial fibrillation.

Conclusion

This survey about AF ablation techniques, strategy, and equipment reveals interesting real-world facts, which warrant further investigation and scientific work: first of all, we have areas of common and standard practice in Europe: paroxysmal and persistent AF ,1 year is the most frequent ablation indication. In paroxysmal AF, PVI is the endpoint of choice induced either with a cooled tip catheter in combination with a 3D navigation system or a cryo-balloon. With the first procedure, success rates are estimated to range between 50 and 70% with >70% including multiple procedures, and nearly 70% without using oesophageal temperature monitoring. But even in this well investigated field of paroxysmal AF, there are areas of variation: 54% of centres do not perform AF ablation as a first-line therapy, whereas the rest is doing so! Pulmonary vein isolation is the standard therapy, but nevertheless five of the interrogated centres do more than PVI in their first ablation for paroxymal AF. In persistent AF, standardization is less well developed: ablation strategy ranging from PVI only to PVI + lines + CFAE is nearly equally distributed and should be a topic for multicentre investigations, which have the power to generate a standard. In addition, estimation of success and amount of post-ablation atrial tachycardias exhibits a wide range, emphasizing the need for more operator training, prospective and randomized data but also for more standardization in follow-up concepts.

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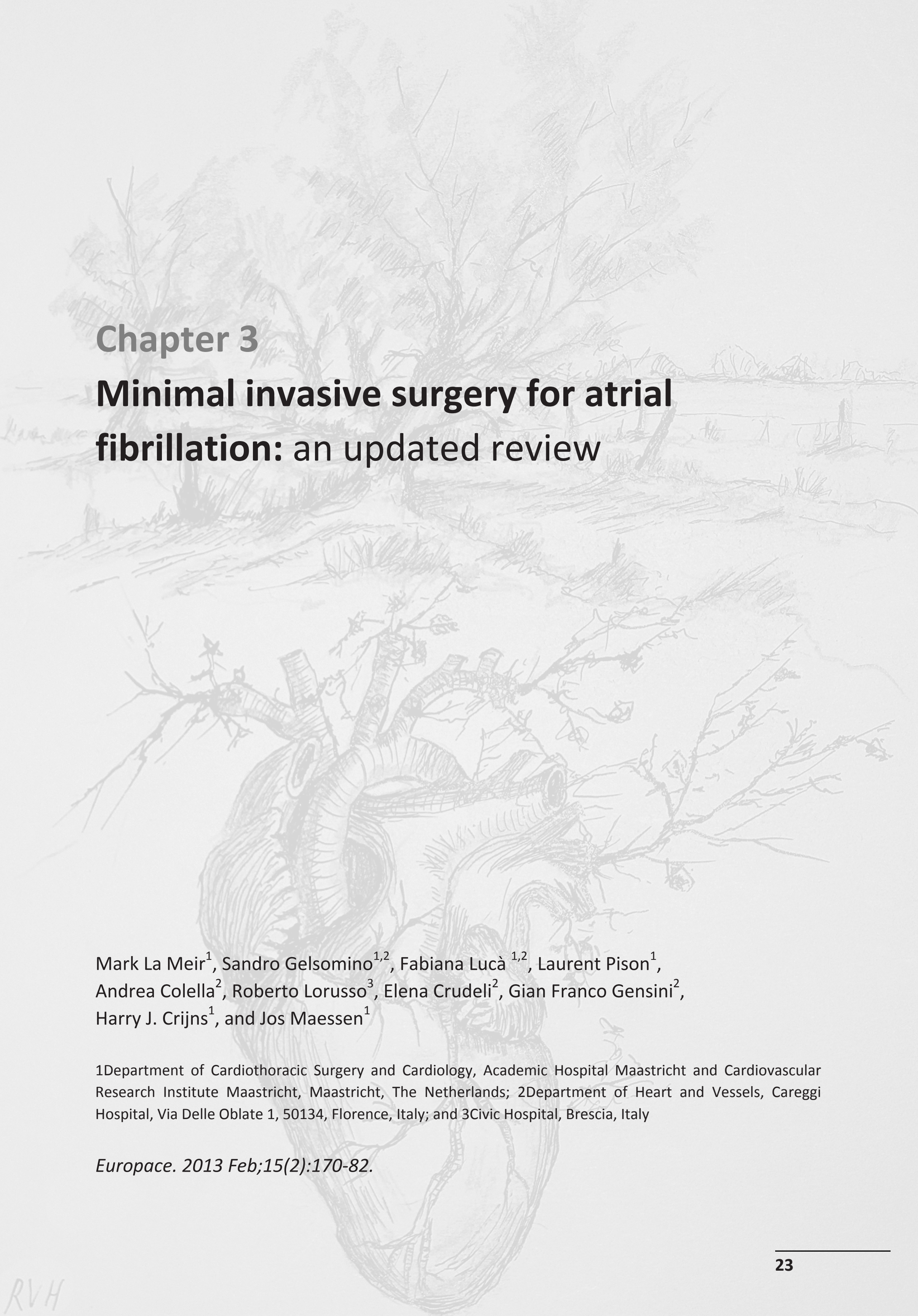
References

1. Calkins H, Kuck KH, Cappato R, Brugada J, Camm AJ, Chen SA et al. 2012 HRS/ EHRA/ECAS Expert Consensus Statement on Catheter and Surgical Ablation of Atrial Fibrillation: recommendations for patient selection, procedural techniques, patient management and follow-up, definitions, endpoints, and research trial design. Europace 2012;14:528–606.
2. Camm J. Antiarrhythmic drugs for the maintenance of sinus rhythm: risks and benefits. Int J Cardiol. 2012;155:362–71.
3. Calkins H. Catheter ablation to maintain sinus rhythm. Circulation 2012;125: 1439–45.



Chapter 3

Minimal invasive surgery for atrial fibrillation: an updated review

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Europace. 2013 Feb;15(2):170-82.

Abstract

Aims

Despite its proven efficacy, the Cox-Maze III procedure did not gain widespread acceptance for the treatment of stand-alone atrial fibrillation (SA-AF) because of its complexity and technical difficulty. Surgical ablation for SA-AF can now be successfully performed utilizing minimally invasive surgery (MIS). This study provides an overview of state-of-the-art MIS for the treatment of SA-AF.

Methods and results

Studies selected for this review were identified on PUBMED and exclusion and inclusion criteria were applied to select the publication to be screened. Twenty-eight studies were included; 27 (96.4%) were observational in nature whereas 1 was prospective non randomized. The total number of patients was 1051 (range 14–114). Mean age ranged from 45.3 to 67.1 years. Suboptimal results were obtained when employing microwave and high focused ultrasound energies. In contrast, MIS ablation of SA-AF achieved satisfactory 1-year results when the bipolar radiofrequency was employed as energy source, with antiarrhythmic drug-free success rate comparable to percutaneous catheter ablation (PCA). The success rate in paroxysmal was even higher than in PCA. In contrast, ganglionated plexi ablation and left atrial appendage removal do not seem to influence the recurrence of AF and the occurrence of postoperative thromboembolic events.

Conclusion

Minimally invasive surgery ablation of SA-AF achieved satisfactory 1-year results when the bipolar radiofrequency was employed. Nevertheless, the relatively high complication rate reported suggest that such techniques require further refinement. Finally, the preliminary results of the hybrid approach are promising but they need to be confirmed.

Keywords

Atrial fibrillation - Ablation - Surgery

Introduction

Over the last 20 years, surgeons and electrophysiologists (EPs) have been making progress towards finding a cure for atrial fibrillation (AF) that offers patients an acceptable risk/benefit profile. The Cox-maze III procedure has been shown to be an effective, but invasive and complex procedure and, for this reason, it has not been widely accepted as a stand-alone therapy.[1,2] Transvenous pulmonary vein isolation (PVI) has become the cornerstone of catheter ablation for AF and is currently the therapy of first choice if patients warrant rhythm control and fail antiarrhythmic drugs (AADs).[3,4] Pulmonary vein isolation is reported to be effective in 60–85% of the patients, especially in patients with paroxysmal short-lasting episodes of AF.[3 – 5] Nevertheless, in about one-third of patients, a second ablation procedure is necessary and complications may occur in up to 6% of patients.[6,7]

The surgical treatment of atrial fibrillation has undergone dramatic changes over the last decade. New technologies have allowed the creation of transmural lesions on a beating heart through alternative, less-invasive incisions.[8] The introduction of these technologies has greatly simplified the performance of the Maze procedure and allowed for the development of minimally invasive surgery (MIS).[8] Minimally invasive video-assisted techniques allow pulmonary vein island creation and left atrial appendage (LAA) removal or exclusion, usually with ganglionic plexus evaluation and destruction.[9] Nevertheless, it is still uncertain whether these procedures are effective in restoring permanent sinus rhythm.[10] We present a systematic literature overview of MIS for the treatment of stand-alone atrial fibrillation (SA-AF) and briefly discuss the hybrid approach which combines, in one-step, off pump epicardial ablation with PVI.

Review criteria

Studies selected for this review were identified on PUBMED (last search 30 September 2011) using the following search terms: ‘stand alone atrial fibrillation’, ‘Mini-Maze’, ‘video assisted’, ‘epicardial ablation’, ‘endoscopic ablation’, ‘videothoracoscopy’, ‘minimally invasive’, ‘surgical ablation’, ‘bilateral thoracoscopic surgical ablation’, ‘right thoracoscopic surgical ablation’, ‘left atrial appendage exclusion’, and ‘ganglionic plexus ablation’. Exclusion criteria were animal studies, reviews, case reports, concomitant surgery, not lone atrial fibrillation, not MIS, not performed on the beating heart, not English, no full-text availability.

These criteria were chosen to make a selection based on title and/or abstract. Inclusion criteria were studies with >10 patients, follow-up of >3 months, minimally invasive beating heart surgery and surgery for lone atrial fibrillation. The search returned a total of 631 papers. A total of 40 articles were selected. Ten met inclusion criteria but were excluded because they had <10 patients.[11 – 20] Two were excluded because ablations were performed on a cardiopulmonary bypass.[21,22] The final selection included 28 studies.[23 – 50]

Definitions

In recent years, it has been hypothesized that SA-AF and pathological AF are different disease processes with contrasting risk predictors.[51] The 2006 ACC/AHA/ESC guidelines stated that there was no standard definition for lone AF.[52] The guidelines applied the term to '. . . individuals younger than 60 years without clinical or echocardiographic evidence of cardiopulmonary disease, including hypertension'.[1,21] A recent international consensus on nomenclature and classification of AF mentions that only AF in the absence of heart disease is termed 'lone' whereas in the absence of any disease it is termed 'idiopathic'.[53] Indeed, lone AF does not necessarily mean 'idiopathic'. By convention, the term 'nonvalvular AF' is restricted to cases in which the rhythm disturbance occurs in the absence of rheumatic mitral valve disease, a prosthetic heart valve, or mitral valve repair.[1] However, the reviewed publications were appraised employing a definition of AF as a stand-alone procedure for treating AF without concomitant surgery.

Baseline characteristics

An overview of the selected studies is presented in Table 1. Studies were published between 2004 and 2011, and 27 of 28 (96.4%) studies were observational in nature whereas one study[42] was prospective non-randomized. Twenty-six studies (89.6%) were performed in a single centre, one study included five centers,[36] one study included three North American Institutions,[35] and one study prospectively enrolled patients from two different centres.[42] Three studies of the groups of Edgerton et al.,[26,31,36] Pruitt et al.,[25,29] Sirak et al.,[32,43] and Cui et al.[41,50] may report on overlapping patients, thus, when discussing results, we refer to their most recent publications. The total number of patients was 1051 (range 14–114). Mean age ranged from 45.3 to 67.1 years. Only two studies had a population with mean age of <50 years.[28,39] Two studies [31,45] did not report the population's age. Atrial fibrillation duration ranged from 0.6 to 12.1 years. Three papers did not report AF duration[44,45,49] and one paper[26] classified patients on the basis of AF duration: <6 months (n = 3), 6–12 months (n = 5), >12months (n = 73), and unknown (n = 2). Only eight papers (34.8%) distinguished long-standing persistent (LSP) AF as requested by recent guidelines[54] and in two studies[43,50] 100% of patients had LSP-AF. A total of 443 patients (42.1%) with paroxysmal AF underwent MIS, 189 (18.0%) had persistent AF, 123 (11.8%) LSP, and 95 (9.0%) permanent, whereas 97 (9.2%) were not clearly defined and one paper reported paroxysmal and persistent AF together (n = 104, 9.9%).[49] Finally, 218 patients (20.7%) had one or more previous percutaneous catheter ablation (PCA). In one paper[40] all patients had at least one PCA before surgery.

Table 1. Minimally Invasive surgery for Lone Atrial Fibrillation: Baseline Characteristics.

First Author	Year	U/M	Pts.	Age	AF duration (y)	LA diameter (mm)	PCA	PX	PR	LSP	PM
Salenger[23]	2004	U	14	60±4	6.9	47.3±7.3	1	10	1	-	3
Wolf[24]	2005	U	29	57.2±14.9	7.5	*	2	18	4	-	5
Pruitt[25]	2006	U	50	59±10	6.1	†	11	‡	‡	‡	‡
Edgerton[26]	2007	U	83	60	§	52	21	72	21	21	-
Mc Clelland[27]	2007	U	20	59±8	1.4	44±3	ns	11	5	4	-
Koistinen[28]	2007	U	22	45.3±10.2	6.6	42.9±5.2	0	10	12	-	-
Pruitt[29]	2007	U	100	60±9	6.0	**	ns	64	11	-	25
Sagbas[30]	2007	U	26	56±11	2.8	42.2±6.3	6	8	-	-	18
Edgerton[31]	2008	U	74	ns	ns	ns	20	46	14	14	-
Sirak[32]	2008	U	32	61±10	7.7	48.2±8.2	ns	0	3	29	-
Wudel[33]	2008	U	22	62±9	3.7	34.7 ± 11.5	7	14	8	-	-
Bagge[34]	2009	U	42	58 [36-71]	7	45 [26-62]	18	28	6	-	9
Beyer[35]	2009	M (3)	100	65±11	4.9	43±6	ns	39	29	-	32
Edgerton[36]	2009	M (5)	114	59.5±10.6	>1 (n=101)	47.2±8.3	24	60	32	22	-
Edgerton[37]	2009	U	30	58±9	>1	52	ns	-	10	20	-
Han[38]	2009	U	45	64±8.7	6.2	43±6	12	33	12	-	-
Klinkemberg[39]	2009	U	15	47±10	5.0	38±5	ns	11	4	-	-
Castella[40]	2010	U	34	54±8.6	8.1	45.3 ±5.6	34††	17	12	5	-
Cui[41]	2010	U	81	58±10	5.9	49.7±11.4	4	49	17	-	15
Edgerton[42]	2010	M (2)	52	60[42-79]	>1	48 [3.7-6.0]	10	52	-	-	-
Sirak[43]	2010	U	48	60±6	4.3	45 [34-63]	13	-	-	48	-
Speziale[44]	2010	U	46	54.9	ns	42±5	14	19	27	-	-
Stamou[45]	2010	U	20	ns	ns	ns	ns	ns	ns	ns	ns
Yilmaz[46]	2010	U	30	55.6±8.6	6.6	ns	18	19	8	-	3
Krul[47]	2011	U	27	57±7	0.6	47±7	14	16	3	2	-
La Meir[48]	2011	U	28	67.1±9.1	12.1	41.6±5.7	21	14	5	9	-
Nasso[49]	2011	U	104	63.9±8	ns	21.3±5 ‡‡	24	104§§	104§§	-	-
Wang[50]	2011	U	83¶¶	57±11	5.1	52.5±11.5	ns	-	-	83	-

Studies were presented by year of publication and in alphabetical order. **Abbreviations:** U/M: Unicentric/Multicentric study; Age expressed as mean ± SD or [range]; AF duration expressed y: years LA : Left atrial; LA Diameter expressed a s as mean ± SD or median [Interquartile range]; PCA: Percutaneous catheter Ablation ; PX: Paroxysmal atrial fibrillation; PR: Persistent atrial fibrillation; LSP: Long-standing Persistent atrial fibrillation; PM: Permanent atrial fibrillation; ns: not specified.

Notes: *†< 60 mm (n=26) > 60mm(n=1); † * < 60 mm (n=26) > 60mm(n=1); †<46 mm (n=23), 46-59 mm(n=24), ≥60 mm (n=3; ‡ AF classified as intermittent (n=33) and continuous (n=17); § <6 m (n=3), 6-12 m (n=5), >12 m (n=73), unknown (n=2).; ¶ Persistent and Long-standing persistent reported together). ** <46 mm (n=42), 46-59 mm(n=53), ≥60 mm (n=5) ; ††All patients had PCA by definition; ‡ ‡indexed by BSA;§§ Paroxysmal and persistent reported together; ¶ ¶ 41 patients treated with irbesartan.

Surgery

Video-assisted thoracic surgery was employed in all studies (Table 2). In their 2006 paper Pruitt et al.[25] performed a robotic-assisted pericardial ablation in 3 of 50 (6%) of patients.

Edgerton et al.,[26,31,36,37,42] McClelland et al.,[27] Beyer et al.,[35] and Stamou et al.[45] carried out a small thoracothomy (4–6 cm) to introduce the endoscopic instruments into the thoracic cavity. Three studies[39,44,49] employed a right monolateral approach where in the others a bilateral access was performed. These authors used monopolar radiofrequency[44,49] or high-intensity focused ultrasound (HIFU). Four studies[23,25,28,29] employed microwave (MW), whereas in the majority of them the energy source was bipolar radiofrequency. Excluding the three right thoracotomy accesses, patients in all studies but one[26] underwent excision/ligation of the LAA. In 15 studies LAA was stapled/legated in all patients. In four studies[23,25,30,36] a variable percentage of patients (16%, 8%, 39% and 11%, respectively) did not have LAA stapler/ligation for unexplained reasons. Only a few groups clearly stated the indications for LAA removal: La Meir et al.[48] performed LAA stapler/clip in patients with CHADS2 score ≥1, in the presence of rapid firing coming from the LAA and when the procedure was deemed safe (50%). Cui et al.[41] did not perform LAA excision in the first 10 patients (12.4%) because of the lack of the appropriate endoscopic equipment and Edgerton et al.[42] did not remove LAA in eight patients (15%) because the procedure was deemed hazardous. Seventeen groups (60.7%) carried out ganglionated plexi (GP) ablation. Additional left atrial lesions are reported in 10 studies. They consisted of a roof line connecting superior pulmonary veins,[26,31,37,47,48] an inferior line connecting inferior pulmonary veins,[47,48] a connecting line between the superior line (or the box) and the left fibrous trigone,[26,31,32,37,43,47] a connecting line from the superior pulmonary vein and the LAA[23,25,26,28,29,31,32,37,43] and a line from the right inferior pulmonary vein to the coronary sinus (CS).[32,43] Additional right lesions are reported in four papers and indications were persistent/long-lasting persistent AF with LA volume >58 mL,[48] permanent/persistent AF,[23] continuous AF[25] or it was not specified.[29] Lesion consisted of a superior vena cava (SVC) to inferior vena cava (IVC) line,[23,25,29,48] a line up to the tip of the right atrial appendage,[23,25,29] or a line towards the CS.[23] La Meir et al.[48] added an SVC circumferential isolation in three cases (to be sure that the SVC-IVC line would not stop at an area of conduction (in patients with a small portion of intrapericardial IVC). These investigators also added a circumferential SVC isolation in case of a rapid firing coming from the SVC (n = 7.1). Klinkenberg et al.[39] added a tricuspid vena cava isthmus line ablation in one patient during reoperation for bleeding. Electrophysiological testing of the lesions was carried out only by Krul et al.[47] In other groups entry and exit block was checked by baseline and post-isolation sensing and pacing.[26,31 – 38,40 – 42,45,46,48 – 50] Speziale et al.[44] measured the conductance across the lesion and a value of <50% than predicted defined an adequate lesion. Finally, McClelland et al.[27] performed ablations guided by epicardial mapping.

Table 2. Minimally Invasive surgery for Lone Atrial Fibrillation: Surgery

First Author	Source	Method	Access	GP	LAA	AL
Salenger [23]	MW	VATS	B	N	Y (9)	Y
Wolf[24]	RF(b)I	VATS	B	N	Y	N
Pruitt[25]	MW	VATS (47) /Rob (3)	B	N	Y(46)	Y
Edgerton[26]	RF(b)I	Thoracotomy /VATS	B	Y	Y	Y
Mc Clelland[27]	RF(b)I	Thoracotomy /VATS	B	Y	N	N
Koistinen[28]	MW	VATS	B	N	Y§	N
Pruitt[29]	MW	VATS	B	N	Y	Y
Sagbas[30]	RF(b)I	VATS	B	N	Y (16)	N
Edgerton[31]	RF(b)I	VATS	B	Y	Y	Y
Sirak[32]	RF(b) NI	VATS	B	Y	Y	Y
Wudel[33]	RF(b)NI	VATS	B	N	Y	N
Bagge[34]	RF(b)I	VATS	B	Y	Y	N
Beyer[35]	RF(b) I NI	Thoracotomy /VATS	B	Y	Y	N
Edgerton[36]	RF(b)I	Thoracotomy /VATS	B	Y	Y(101)	N
Edgerton[37]	RF(b)I	Thoracotomy /VATS	B	Y	Y	Y
Han[38]	RF(b)I	VATS	B	Y	Y	N
Klinkemberg[39]	HIFU	VATS	R	N	N	Y*
Castella[40]	RF(b) NI	VATS	B	Y	Y	N
Cui[41]	RF(b) NI	VATS	B	N	Y (71)	N
Edgerton[42]	RF(b)I	Thoracotomy /VATS	B	Y	Y(44)	N
Sirak[43]	RF(b)I	VATS	B	Y	Y	Y
Speziale[44]	RF(m)	VATS	R	N	N	N
Stamou[45]	RF(b) I NI	Thoracotomy	B	Y	Y	N
Yilmaz[46]	RF(b) NI	VATS	B	Y	Y	N
Krul[47]	RF(b) NI	VATS	B	Y	Y	Y
La Meir[48]	RF(b)I	VATS	B	Y	Y (14)	Y
Nasso[49]	RF(m)	VATS	R	N	N	N
Wang[50]	RF(b) NI	VATS	B	Y	Y	N

Studies were presented by year of publication and in alphabetical order **Abbreviations:** GP: Ganglionated plexi (ablation); LAA: Left atrial appendage excision/closure; AL: Additional lines; Source: MW: Microwave; RF: Radiofrequency; Cryo: Cryotherapy; HIFU: High-Intensity Focused Ultrasound b: bipolar; u: unipolar; I. Irrigated; NI: Not irrigated; VATS: video assisted thoracoscopic surgery; Rob: Robotic-assisted surgery; ns: not specified.

Notes: * during reoperation for bleeding a tricuspid-vena cava inferior isthmus ablation was performed in one pt. † Eight underwent additional mitral and tricuspid procedures ; ‡ Performed on Cardiopulmonary bypass; § LAA was excised if it was deemed to be significantly enlarged or if the patient had suffered from a thrombo-embolic event.

Follow-up, rhythm monitoring, anticoagulation, and antiarrhythmic therapy

One thousand onehundred ninety-nine patients (87.4%) reached the maximum follow-up which was 100% complete in 13 papers (46.4%). In the others the follow-up completeness ranged from 32% to 95% (Table 3). The longest follow-up was 36 months[48] and nine studies reported a follow-up of <12 months which is the minimum recommended for evaluating procedural efficacy.[4] Excluding two which did not mention any continuous rhythm monitoring[23,45] and one which performed electrophysiological studies,[25] all the others papers employed at least one method of long-term monitoring. Fifteen studies (53.5%) utilized 24 h Holter monitoring (HM) at different intervals,[28,33,35,40,41,44,46,47,49,50] two 24–48 monitoring,[34,39] one 7-day HM[48] and one 30-day HM[27] and in one it was not specified. In five (17.8%) studies HM was associated with another long-term monitoring: 14- to 21-day event recorder in Edgerton et al.[26,31,36,42] and outpatient telemetry (OT) in Sagbas et al.[30] Among studies which did not utilize HM, OT,[24,43] event monitoring,[32,37]and trans-telephonic monitoring associated with event monitoring were the methods for rhythm assessment. Only a few papers clearly described the adopted protocol for AADs during the follow-up: AADs were withdrawn in patients in sinus rhythm (SR) after 3 months in seven studies,[22,23,40,41,44,47,48] at 6 months in two studies,[30,42] and two more studies stated that AADs were stopped after demonstration of stable SR at 3- and 6-month visits.[44,49,50] Sirak et al.[32] and Yilmaz et al.[46] reported that AADs were withdrawn at the discretion of the referring cardiologist. Similarly, a standard protocol was not followed for oral anticoagulation (OA) therapy: it was discontinued at three months by Salenger et al.[23] and La Meir et al.[48] {if CHADS2 [cardiac failure, hypertension, age, diabetes, stroke (doubled)] score was <2}, at 4 months by Cui et al.,[41] at 6 months by Sagbas et al.,[30] Edgerton et al.,[37] Han et al. (if CHADS2 score was <2)[38] and Klinkenberg et al.,[39] at 6 months to 1 year by Castella et al.[40] and at 1 year by McClelland et al.[27] Furthermore, in Wudel et al.[33] and Yilmaz et al.[46] anticoagulants were discontinued at the discretion of the referring cardiologist: Speziale et al.[44] and Nasso et al.[49] kept patients under OA until SR was maintained for 3 months, whereas Krul et al.[47] discontinued OA when CHADS2 score was <1 without AF and AAD. Finally, Wang et al.[50] continued OA for at least 3 months. Patients taking AADs at latest follow-up were shown or could be calculated in 22 of 28 (78.5%) studies. The range was from 2% to 53% (mean 26±15%). Patients still under OA therapy at follow-up could be obtained from 15 of 28 (53.5%) studies. The range was from 0% to 63% (mean 39±19%). Quality-of-life assessment was carried out employing the 36-item short form health survey questionnaire by Speziale et al.[44] and Nasso et al.,[49] both showing an improvement in all indexes with the exception of vitality score. Pruitt et al.[25,29] explored the perceived health status after surgery: 81.8% and 52.3% of patients were pleased with the outcome and 81.8% and 55.7% felt the operation had been beneficial, in the two publications, respectively.

Table 3. Minimally Invasive surgery for Lone Atrial Fibrillation: End-points and Rhythm Monitoring

First Author	F-Up (m)	End-point	N (%)	F-Up type	Rhythm Monitoring	AAD	OA
Salenger [23]	12	1	14 (100)	OC	ns	ns	ns
Wolf2 [24]	6	1	23(79)	OC-MR-TI-CV (3-5-6 M)	ECG (10) OT(13)	9	ns
Pruitt [25]	7.6	2	44 (88)	OC-TI (ns)	ECG EPS	20	50
Edgerton [26]	6	3	57 (69)	OC(1-3-6 M)	ECG, 14-21-day event recorder (24)24HM (24), Pm (9)	34	ns
Mc Clelland [27]	17±3	4	20 (100)	OC(1-2-3-6-W 3-6 M-every 6M)	*30-day HM (12M)	25	ns
Koistinen [28]	11.5±6	2- 5	22 (100)	OC (1-3-6 M)	24HM (6M)	2	0
Pruitt [29]	23.1	6	88 (88)	OR-MR-EPS (ns)	ECG -HM (ns)	11	54
Sagbas [30]	8±3	2	26 (100)	OC (3-6 M)	OT; 24HM (ns)	19	54
Edgerton [31]	6	3	66 (89)	0C (1-3-6 M)	ECG; 14-21-day event recorder (ns)24HM (ns)	47	ns
Sirak [32]	6	1	19(40)	OC	7-day event recorder (3-6-13-24M)	ns	ns
Wudel [33]	18± 4	2	22 (100)	OC (3-6-12 M)	24HM (ns)	9	9
Bagge [34]	12	1	41 (78)	OC (3-6-12-M)	24-48HM (ns)	32	24
Beyer [35]	13±8	7	100 (100)	0C (3M –every Year)	24HM (3M)	37	36
Edgerton [36]	17±3.4	1	114(100)	OC (1-3-6 M)	24 HM (26) 14- 21-day event recorder (68) Pm (15)	43	ns
Edgerton [37]	6	8	30 (100)	OC (1-3-6 M)	ECG-Event Recorder Pm	53	47
Han [38]	12	9	43 (95)	OC (6-12 M – Yearly)	30-day event recorder (6m) TTM (12M)	35	33
Klinkemberg [39]	1.3±0.6 y	10	15 (100)	OC (2-6—12--24M)	ECG 24HM (2m) 48 HM (6m)	40	ns
Castella [40]	16±11	11	11 (32.3)	OC (1-4-6-12 M)	ECG 24HM (4-6M-1Y)	ns	63
Cui [41]	12	11	49 (60)	OC (1-3-6-12 M)	ECG, 24-48 HM, Pm ,UCG	ns	ns
Edgerton [42]	12	8	52 (100)	OC (1-3-6-12 M)	24 HM 14-21-day event recorder Pm	11	19
Sirak [43]	6	7	24 (75)	OC (3-6-13 M)	OT	12	ns
Speziale [44]	9.3±3.2	3	46(100)	OC (3-6 -12 M)	ECG 24HM (6-12 M)	ns	ns
Stamou [45]	12	ns	12 (60)	ns	ns	ns	ns
Yilmaz [46]	11±4	7	30 (100)	OC(1-3-6-W 3-6-12M)	ECG 24HM (3-6-12 M)	35	52
Krul [47]	12	12 -9	22(71)	OC (3-6-12-15-18-24 M)	ECG 24HM (every 3 M)	14	48
La Meir [48]	36	13	24(85.7)	OC(2-W 1-6-12M-Yearly)	ECG 7day-HM(2-W 1-6-12M-Yearly)	11.3	15.2
Nasso [49]	17±6	1- 5	104(100)	OC (3-6 –every 6 M)	ECG, 24HM(3-6 M)	49	60
Wang [50]	26	11	81 (97.5)	OC (1-3-6-12 M-every 6 M)	ECG 24-48 HM (3M)	21	ns

Studies were presented by year of publication and in alphabetical order. **Abbreviations**: F-Up: Follow-up; m=months; N (%): Number (percentage) of patients at follow-up; ADD: (%patients taking) Antiarrhythmic Drugs; OA : (%patients taking) Oral Anticoagulants. **Endpoint**: 1= freedom from AF,2=number of patients in sinus rhythm/with no AF; 3: No episodes of AF >15 sec at 6 months 4: Free of AAD (Class IC and III) and AF , no > 30 sec of AF ; 5: episodes of AF, 6: Absence of AF on all serial ECG, Holter Monitoring or 30-day event –free monitoring >6 months after procedure; 7: No episode of AF o left Atrial Tachyarrhythmia (AT) after blanking period of 3 months;8:No AT, AF or Atrial Flutter (AFl) >30 seconds during monitoring at 6 months; 9: No AT, AF or Atrial Flutter (AFl) lasting >30 seconds off antiarrhythmic drugs, 10: Absence of AF AFl and AT on 96h HM or ECG >30 sec and no AF compliant; 11: No AF or Atrial Flutter (AFl) >30 seconds during ECG or Holter

Monitoring:; 12: Freedom from AT, AF or Afl off antiarrhythmic drugs after 12 months;13: Time-related prevalence of AF (defined as of AF o left Atrial Tachyarrhythmia after blanking period of 3 months. **Follow-Up type**: OC: Outpatient Clinic; MR: Medical Records; TI: Telephonic Interviews;; CV: Cardiologic Visits; M: Months; ns: not specified; **Rhythm Monitoring**: ECG: Electrocardiograms HM: Holter Monitoring;, , OT : Outpatient (Cardiac) Telemetry; TTM : Trans Telephonic (event) Monitor Pm= Pace-maker; UCG: Ultrasonic Cardiographic evaluation, EPS: Ectrophysiology studies ; **Notes**: * 1 Patient underwent 15-day HM.

Results

Only six papers,[27,34,38,42,47,50] all utilizing radiofrequency, clearly defined the primary efficacy endpoint of surgery as suggested by current guidelines [freedom from AF, off AADs at 1 year (Table 4)].[4] The follow-up was 93.3% complete (251 of 269 patiens) and the success rate ranged from 51% to 86%. One study reported a 2-year success rate of 80%. With specific reference to the different type of AF, AAD-free success rate at 12 months ranged from 65% to 92% in paroxysmal AF and from 67% to 80% in persistent AF. Only three studies[27,47,50] reported 12-month AAD-free success rate in LSP [25% (4 patients at follow-up), 100% (1patient at follow-up), and 80% (81patients at follow-up)]. Eight studies[26,30 – 33,35 – 37] reported outcomes as freedom from AF and AAD at 6 months (Table 5). This rate ranged from 57% to 91% in the whole population, from 72% to 100% in paroxysmal and from 35%to 78% in persistent AF. Two papers[36,37] showed this outcome in LSP patients [32% (22 patients at follow–up) and 47% (15 patients at follow-up)] and one report[30] showed AAD-free in permanent AF (72% (18 patients at follow-up)]. Wolf et al.[24] Yilmaz et al.[46] and Nasso et al.[49] reported freedom from AF-AAD at different intervals (Table 6): 65% beyond 3-month follow-up, 65% at 12.6-month follow-up, and 51% at 17.1-month follow-up, respectively.

Three papers showed outcome as 12-month freedom from AF (62% and 75%, respectively)[40,45] or 3-month freedom from AF (100%).[43] Furthermore, in two publications[41,44] 80% (39 of 49) and 87% (40 of 46) of patients are in sinus rhythm at 12 and 6 months, respectively (Table 6). La Meir et al.[48] employed a method suggested by the Workforce on Evidence-Based Surgery of the Society of Thoracic Surgeons, reporting time-related prevalence of AF[55] (Table 6). Four studies employing MW[23,25,28,29] reported a freedom from AF success rate of 67%, 79.5%, 86%, and 42%, respectively. One group utilizing HIFU[39] reported a 6-month AF-AAD-free success rate of 33% (Table 7). Krul et al.[47] carried out a roof and inferior line with 86% 1-year freedom from AF-AAD (22 patients). It was 100% for Sirak et al.[43] (19 patients all LSP) and 58% for Edgerton et al.[31](24 patients) at 6 months. In three studies utilizing MW[23,25,29] an additional line towards LAA was performed. Unfortunately none of these papers reports AAD-free rate. Groups performing GP ablation reported a 6-month and 12-month AAD-free success rate ranging from 51% to 86% and 58% to 88%, respectively. Two studies employing bipolar radiofrequency[30,33] without GP ablation reported an AAD-free success rate of 81% and 91%, respectively.

Table 4. Minimally Invasive surgery for Lone Atrial Fibrillation with Radiofrequency: Studies Reporting Results According HRS/EHRA/ECAS Consensus (Freedom from AF , off antiarrhythmic drugs (ADD) at one year.

	ALL			Paroxysmal			Persistent			LS-Persistent			Permanent		
First Author	**n**	**AF**	**AF-AAD**	**n**	**AF**	**AF-AAD**	**n**	**AF**	**AF-AAD**	**n**	**AF**	**AF-AAD**	**n**	**AF**	**AF-AAD**
MClelland[27]	5	75(15/20)	75(15/20)	1	91(10/11)	91(10/11)	1	80(4/5)	80(4/5)	3	25(1/4)	25(1/4)	-	-	-
Bagge[34]	8	76(25/33)	51 (17/33)	5	79 (19/24)	ns	0	100 (2/2)	ns	-	-	-	3	54 (4/7)	ns
Han[38]	15	65 (28/43)	65 (28/43)	11	65 (20/31)	65 (20/31)	4	67 (8/12)	67 (8/12)	-	-	-	-	-	-
Edgerton[42]	10	81 (42/52)	73 (38/52)	10	81 (42/52)	73 (38/52)	-	-	-	-	-	-	-	-	-
Krul[47]	2	91 (20/22)	86 (19/22)	0	100(12/12)	92 (11/12)	2	78 (7/9)	78(7/9)	0	100 (1/1)	100(1/1)	-	-	-
Wang[50]	15	80 (65/81)	80 (65/81)	-	-	-	-	-	-	15	80 (65/81)§	80 (65/81)§	-	-	-

Studies were presented by year of publication and in alphabetical order. **Abbreviations:** HRS: Heart Rhythm Society; EHRA: European Heart Rhythm Association; ECAS: European Cardiac Arrhythmia Society ;AF: (patients free of) Atrial fibrillation; AF-AAD (Patients free of) Atrial Fibrillation and Antiarrhythmics, ns: not specified.
Notes: *AF defined as intermittent or continuous † Persistent and Long –standing persistent presented together.

Table 5. Minimally Invasive surgery for Lone Atrial Fibrillation with Radiofrequency: Studies Reporting Results with Freedom from AF , off antiarrhythmic drugs (ADD) at 6 months

	ALL			Paroxysmal			Persistent			LS-Persistent			Permanent		
First Author	**n**	**AF**	**AF-AAD**	**n**	**AF**	**AF-AAD**	**n**	**AF**	**AF-AAD**	**n**	**AF**	**AF-AAD**	**n**	**AF**	**AF-AAD**
Edgerton[26]	15	74(42/57)	63(36/57)	7	82(32/39)	74(29/39)	8	56(10/18)	39(7/18)	*	*	*	-	-	-
Sagbas[30]	5	81 (21/26)	81 (21/26)	0	100(8/8)	100(8/8)	-	-	-	-	-	-	5	72(13/18)	72(13/18)
Edgerton[31]	17	74(49/66)	58(38/66)	7	84 (36/43)	70 (30/43)	10	57(13/23)	35(8/23)	ns	ns	ns	-	-	-
Sirak[32]	3	88(21/24)	88(21/24)	-	-	-	ns	ns	ns	ns	ns	ns	-	-	-
Wudel[33]	9	91(20/22)	91(20/22)	ns	ns	ns	ns	ns	ns	-	-	-	-	-	-
Beyer[35]	13	87 (87/100)	63 (63/100)	5	87 (34/39)	ns	0	100 (29/29)	ns	-	-	-	9	72 (23/32)	ns
Edgerton[36]	33	71(81/114)	57(65/114)	8	87 (52/60)	72 (43/60)	14	56(18/32)	47(15/32)	11	50(11/22)	32 (7/22)	-	-	-
Edgerton[37]	6	80 (24/30)	58(14/24)	-	-	-	1	90 (9/10)	78(7/9)	5	75 (15/20)	47 (7/15)	-	-	-
Sirak[43]	0	100 (19/19)	100 (19/19)	-	-	-	-	-	-	0	100 (19/19)	100 (19/19)	-	-	-

Studies were presented by year of publication and in alphabetical order. **Notes**: * Persistent and Long –standing persistent presented together.

Table 6. Minimally Invasive surgery for Lone Atrial Fibrillation with Radiofrequency: Studies Reporting Results with alternative follow-up

	ALL			Paroxysmal			Persistent			LS-Persistent			Permanent		
First Author	**n**	**AF**	**AF-AAD**	**n**	**AF**	**AF-AAD**	**n**	**AF**	**AF-AAD**	**n**	**AF**	**AF-AAD**	**n**	**AF**	**AF-AAD**
Wolf[24]	2	91 (21/23)	65 (15/23)	1	ns	ns	0	ns	ns	-	-	-	1	ns	ns
Castella[40]	10	62 (16/26)	ns	2	82(9/11)	ns	4	60 (6/10)	ns	4	20 (1/5)	ns	-	-	-
Cui[41]	10	80 (39/49)	ns	ns	80 (ns)	ns	ns	75 (ns)	ns	ns	67 (ns)	ns	-	-	-
Sirak[43]	0	100 (19/19)	ns	-	-	-	-	-	-	0	100 (19/19)	ns	-	-	-
Speziale[44]	6	87(40/46)	ns	1	95(18/19)	ns	5	81 (22/27)	ns	-	-	--	-	-	-
Stamou[45]	3	75 (9/12)	ns	0	100(7/7)	ns	2	40(3/5)	ns	-	-	-	-	-	-
Yilmaz[46]	7	77 (23/30)	65 (19/30)	3	84 (16/19)	ns	2	75 (6/8)	ns	ns	ns	ns	2	33(1/3)	ns
La Meir[48]	-	4.5%	11.3%	-	0%	-	-	0%	100 (8/8)	-	8.3%	50 (3/6)	-	-	-
Nasso[49]	11	89(93/104)	51(53/104)	2	96 (ns)	ns	9	80(ns)	ns	-	-	-	-	-	-

Studies were presented by year of publication and in alphabetical order. **Abbreviations:**AF: (patients free of) Atrial fibrillation; AF-AAD (Patients free of) Atrial Fibrillation and Antiarrhythmics, ns: not specified.

Notes: ‡Published as 36-month time-related prevalence.

Table 7. Minimally Invasive surgery for Lone Atrial Fibrillation: Freedom from Atrial Fibrillation Recurrence and Antiarrhythmic Drugs after microwave ablation.

	ALL			Paroxysmal			Persistent			LS-Persistent			Permanent		
First Author	**n**	**AF**	**AF-AAD**	**n**	**AF**	**AF-AAD**	**n**	**AF**	**AF-AAD**	**n**	**AF**	**AF-AAD**	**n**	**AF**	**AF-AAD**
Salenger [23]	ns	67 (ns)	ns	ns	ns	ns	ns	ns	ns	-	-	-	ns	ns	ns
Pruitt[25]	9	79.5(35/44)	ns	*	*	*	*	*	*	*	*	*	*	*	*
Koistinen[28]	9*	86 (13/22)	63 (10/22)	ns	ns	ns	ns	ns	ns	-	-	-	-	-	-
Pruitt[29]	51	42 (37/88)	ns	ns	ns	ns	ns	ns	ns	-	-	-	ns	ns	ns
Klinkemberg[39]	8	47(7/15)	33(5/15)	5	54 (6/11)	27(4/15)	3	25 (1/4)	25(1/4)	-	-	-	-	-	

Studies were presented by year of publication and in alphabetical order. **Abbreviations:** AF: (patients free of) Atrial fibrillation; AF-AAD (Patients free of) Atrial Fibrillation and Antiarrhythmics, ns: not specified. **Notes**: *AF defined as intermittent or continuous.

Adverse events

Three early deaths have been reported (Table 8): one[26,31,36] occurred during the procedure as a consequence of tearing of LAA, one[41] was due to cerebral infarction and for one death whose cause was unknown.[36] Overall, early complications occurred in 125 patients and the complication rate ranged from 0% to 39%. Early complications were as follows: 12 conversions to sternotomy, 15 bleedings, 10 access-port complications, 11 cardiac complications, 8 cerebrovascular events, and 28 pulmonary complications. Furthermore, 38 other complications occurred: 4 renal insufficiencies, 16 diaphragmatic-phrenic nerve dysfunctions, 1 liver damage, and 4 brachial plexopathies were observed. Finally, 10 patients required a pacemaker implantation and two patients underwent PCA within 30 days (Table 8). Three deaths occurred during the follow-up and none was cardiac related: one unexplained death[25] occurred in an obese patient who had severe pulmonary disease at the time of operation, one patient died from trauma and one from malignant neoplasm.[46] Other complications included cerebrovascular accident (n = 4), thromboembolic event (n = 1), anticoagulation-related complication (n = 1), and post-pericardiotomy syndrome (n = 1). In addition, during the follow-up, 27 patients underwent PCA, 13 surgical Cox-Maze, 5 had pacemaker implantations, and 1 patient was rehospitalized for congestive heart failure and atrial flutter.

Table 8. Minimally Invasive surgery for Lone Atrial Fibrillation: Adverse events.

First Author	N	%	Death	Conversion	Bleed	Port	Cardiac	Cerebral	Pulmonary	Other	Late
Salenger [23]	4	28.5	0	2	0	0	0	0	PN; PE	0	PCA(2[3-6-M]); PM([9M])
Wolf[24]	3	13.0	0	0	0	0	Pe	0	PX	Phl	RH
Pruitt[25]	2	4	0	0	0	0	0	0	0	D (2)	Death (1) C-MZ (5)
Edgerton[26]	4	4.8	1[†]	0	0	0	0	0	H	RI; BP	0
Mc Clelland[27]	1	0.5	0	0	0	0	0	0	H	0	PCA (3[ns])
Koistinen[28]	5	2.2	0	0	2	0	0	0	0	Liv.Dam D (2)	PM ([ns])
Pruitt[29]	13	13	0	0	2	0	0	CVA	0	D(7) PM (3)	4CVA, ACC C-MZ (9)
Sagbas[30]	2	7.6	0	0	0	0	0	0	PLE	D	0
Edgerton[31]	4	5.4	1[†]	0	0	0	0	0	H	RI; BP	0
Sirak[32]	1	3.1	0	1	0	0	0	0	0	0	PCA (5 [within 3 M])
Wudel[33]	2	9	0	0	0	Rev	0	0	PE	0	PCA (1[7M])
Bagge[34]	17	39	0	0	6	Rib I (4)	VT PP	Dis Stroke	H (2)	0	PP INF Esoph He (ns)
Beyer[35]	13	13	0	0	0	0	0	TIA	H (3) PE	PM (5) Phre (3)	ns
Edgerton[36]	15	13	2[†]	0	1	0	Pe VT (2)	0	RD (5)	RI (2) Phre BP	ns
Edgerton[37]	0	0	0	0	0	0	0	0	0	0	PM(2) PCA (ns)
Han[38]	0	0	0	0	0	0	0	0	0	0	PCA (8 [532±73 days]) PM
Klinkemberg[39]	3	20	0	0	2*	0	Pe	0	0	0	PCA (6)
Castella[40]	5	14.7	0	0	2	0	0	Stroke	H PAV	0	ns
Cui[41]	6	7.4	1	1	0	Rev (2)	MI	0	Reint	0	ns
Edgerton[42]	4	7.6	0	0	0	0	0	0	0	BP, PM PCA(2)	0
Sirak[43]	2	4.2	0	1	0	0	0	0	0	PM	PCA
Speziale[44]	1	1.9	0	1	0	0	0	0	0	0	0
Stamou[45]	3	15	0	0	0	0	Pe (3)	0	0	0	ns
Yilmaz[46]	4	13.3	0	2	0	0	0	0	PX(2)	0	0

First Author	N	%	Death	Conversion	Bleed	Port	Cardiac	Cerebral	Pulmonary	Other	Late
Krul[47]	6	22.2	0	3	0	0	0	0	H PX PN	0	0
La Meir[48]	0	0	0	0	0	0	0	0	0	0	0
Nasso[49]	3	2.9	0	1	0	0	0	TIA Stroke	0	0	Death (2) TEE
Wang[50]	4	4.8	0	-	-	Rev (2)	-	Stroke	Reint	-	-

Studies were presented by year of publication and in alphabetical order. **Abbreviations:** N: Number of in-hospital complications; %: Percentage of in-hospital complications; **Bleed**: Bleeding; **Port (**access port complications): Rev: Surgical Revision; Rib: Rib Fracture; **Cardiac**: VT: Ventricular tachycardia, Pe : Pericarditis/Pericardial effusion; Myocardial Infarction; **Cerebral:** CVA: Cerebro-vascular Vascular Accident; Dis: Disorientation/Confusion TIA: Transient Ischemic Attack; **Pulmonary:** PN: Pneumonia; PE: Pulmonary Embolism; PX: Pneumothorax; PLE: Pleural Effusion; H: Hemothorax; RD: Respiratory Distress; PAV: Prolonged assisted ventilation; Reint: Reintubation. **Other:** Phl: Phlebitis, D: Diafragmatic dysfunction, RI: Renal insufficiency; BP: brachial plexopathy; PM: Pacemaker implantation, Phre: Phrenic nerve injury, PCA: Percutaneous Catheter Ablation. **Late**: PM: Pacemaker implantation, RH: Re-hospitalization C-MZ: Cox Maze procedure; CVA: Cerebrovascular Vascular Accident, PCA: Percutaneous Catheter Ablation, ACC : Anticoagulation Complications, PP: Post-perdicardiotomy syndrome, INF: Infection; Esoph: Esophagitis He : Portal hernia, TEE: Thromboembolic event, ns: not specified (n of events [time]).

* during reoperation for bleeding a tricuspid-vena cava inferior isthmus ablation was performed in one of these pts.† referring to the some patients.

Discussion

The key purpose of this review is to summarize and discuss published articles about MIS for the treatment of SA-AF. From this overview it is evident that results employing MW energy are rather poor. Indeed Pruitt et al.[29] in the most recent paper report a 42% rate with AAD at 12 months. Microwave is an unfocused heat energy which can create transmural endocardial lesion but it is not capable of creating epicardial lesion on the beating heart[8] and this may explain such unsatisfactory results. In addition, results with HIFU energy were also suboptimal: Klinkenberg et al.[39] reported a 6-month AAD-free success rate of 33%. Indeed, this energy source appears capable of creating endocardial lesions on the arrested heart but has not been able to create transmural lesion on the beating heart and this explains the poor outcome of this study. Bipolar radiofrequency is the most commonly adopted energy source for MIS as it has been demonstrated to produce permanent transmural linear lesions on the beating heart.[8] Two groups performed surgery through a monolateral right thoracotomy approach[44,49] with a success rate without AAD of 51% and with AAD of 87% and 89%. The monolateral approach should significantly lower the possible complication rates (bleeding, pulmonary complications), should be less painful for patients and allow potentially faster recovery. Nevertheless, only monopolar devices were used because of the lack of maneuverability of bipolar clamps which can hamper the orientation of the probe and constrain the variety of achievable lesion sets when employed from the right side. There is concern about the ability of these devices to create transmural lesion with bidirectional conduction block on the beating heart.[56] Further studies are necessary to establish whether this approach may represent a reliable alternative to bilateral bipolar surgical ablation.

Among studies utilizing radiofrequency, freedom from AF-AAD at 12 months ranged from 51% to 86%; this figure was 65-92% in paroxysmal and 67-80% in persistent. Wang et al.[50]reported 80% AF-AAD freedom with 81 patients reaching 1-year follow-up. These results are comparable to those following PCA.[57] Indeed, an updated worldwide survey[7] reported a success rate free of AAD after PCA of 69.9%. It was 71.4% in paroxysmal, 59.4% in persistent, and 59.7% in LSP. Similarly, MIS was more effective in paroxysmal and four of seven studies[27,38,42,47] showed an AAD-free success rate higher than PCA. However, MIS also had better results in persistent in three of three studies reporting AAD-free success rates. In contrast, the success rate was lower in two of three studies in LSP AF. Furthermore, authors performing left additional lines had very high AAD-free success rates in persistent and LSP. This confirms that persistent and LSP AF cannot be successfully treated by PVI alone as the mechanisms for initiation and maintenance of AF lie in the changed left atrial substrate beyond the PVs. From a pathophysiological perspective, this is explained by structural and electrical remodelling of the atrial myocardium, which can then initiate and sustain AF independent of the PVs in patients with persistent/LSP AF. In these patients, the augmented number and location of drivers for fibrillation necessitates additional linear ablation strategies. Another interesting finding of this overview is that from the analysis of the reported results, it seems that GP ablation is not an essential part of the MIS of SA-AF to prevent recurrence of AF. Indeed, groups performing GP ablation reported a 12-month AAD-free success rate lower than studies not performing GP ablation. The long-term efficacy of GP ablation has been questioned[58] and this was related to the possibility of autonomic ganglia to potentially reconnect or regrow.[59] Nevertheless, these data must be interpreted with caution because of the small number of studies with full results available and the short follow-up, and the role of GPs and their destruction in AF must be further investigated.

Mortality rate was low and comparable to PCA (0.4%).[54] Postoperative complication rates are not negligible and higher than PCA.[54] Pulmonary problems, bleeding, and diaphragm/phrenic nerve dysfunction were the most common complications. Nevertheless, the occurrence of transient ischaemic attack/stroke was very low and less than that reported in catheter-based PVI.[54] Interestingly, the incidence of cerebrovascular accidents was not different with or without LAA removal, and from these findings, it seems that this procedure is not a critical component of MIS. However, this finding must be interpreted with extreme caution due to the small number of publications and the lack of uniform anticoagulation policy. Certainly, it is necessary to clearly define the role of LAA removal in MIS ablation as the LAA exclusion/closure is a potentially dangerous procedure and most of the reported bleedings were related to this maneuver. Unfortunately, no randomized control trials have been published comparing MIS with PCA. At the moment there are two ongoing studies: the SCALAF success trial which compares the efficacy of circumferential pulmonary vein ostia ablation using surgical vs. catheter techniques in the treatment of paroxysmal atrial fibrillation, and the FAST II trial that explores whether mini invasive thoracoscopic radiofrequency is more effective compared with a percutaneous catheter-based technique in patients with symptomatic paroxysmal atrial fibrillation refractory to at least one AAD.

The results of these studies will provide a great understanding of the role of both procedures in the treatment of SA-AF. In our recent paper[60] we had given an overview of medical and surgical treatments of atrial fibrillation. This study is mainly focused on providing a more detailed oversight of efficacy and complications of minimally invasive procedure. Krul et al.[61] have recently published a review on the mini-Maze. They included only papers employing radiofrequency and performed an aggregate patient data meta-analysis to compare published results. Our approach was different and we choose to give to the readership as much information as possible to allow them to make their own opinion about the effectiveness/safety of these procedures. Furthermore, we believe that although a well-designed meta-analysis can provide valuable information for researchers, there are too many critical caveats in performing and interpreting it which, therefore, can yield misleading information[62] in particular when individual patient data (IPD) are not available.[63] Indeed, IPD meta-analysis offers advantages and, when feasible, should be considered the best opportunity for summarizing the results of multiple studies. However, the resources, time, and cooperation required for such studies will continue to limit their use in many important areas of clinical medicine which can be meaningfully and cost-effectively approached only by aggregate patient data-based meta-analyses.

Towards a multi-disciplinary approach: the hybrid procedure

With the development of new tools and advanced techniques, the treatment of SA-AF moves towards a multidisciplinary approach involving cardiac surgeons and EPs.[45] The rationale of the so-called 'hybrid' approach is to combine, in one step, a minimally invasive epicardial technique with a percutaneous endocardial ablation in order to limit the shortcomings of both techniques and, at the same time, to combine their advantages. The potential for improved outcomes derives from combining levels of expertise. Surgeons are very good at making linear lesions and EPs at mapping for completeness. Lesions are more likely to be transmural when burning from the inside outwards and from the outside inwards simultaneously and the EP can add an endocardial 'touch-up' in the case of incomplete isolation of one of the pulmonary veins or if the connecting lesions are not transmural.

Furthermore, as discussed above, a more extensive lesion set beyond PVI to include targets along the LA substrate is often necessary in persistent and LSP AF. Nevertheless, while the other lesions can be performed through the transverse sinus, the biggest challenge in the case of the full beating heart is making the connection to the mitral annulus, and this for different reasons: first, the visualization behind the LA of the full beating heart is very limited; second, there is the risk of collateral damage to the circumflex artery; third, the CS, which is used as the epicardial landmark for the mitral annulus, is unreliable and may leave a gap.[64] An attempt to address this problem was made by Edgerton et al.[37] who developed the 'Dallas lesion' in which a line was made connecting to the anterior annulus at the junction of the left and noncoronary cusps of the aortic root. Nevertheless, this line might not be transmural due to the inability of radiofrequency energy effectively to penetrate fatty tissue associated with the dome of the left atrium and the SVC. This is an indication for mapping conduction block which can be checked by using a hybrid approach. In contrast, mitral isthmus lesion can easily be carried out (or completed) endocardially by the EP. Another potential advantage of the hybrid technique is that, from the EP's point of view, there is no longer a risk of phrenic nerve and oesophageal injury because these structures can be protected by the surgeon if necessary, as well as no risk of tamponade as the pericardium is open. Furthermore, by reducing the total number of endocardial ablations the risk of emboli during these ablations should be potentially reduced.[65] A potential drawback of the single-step approach is the patient's heparinization after the transseptal puncture which could increase the risk of epicardial bleeding and the risk of measuring a temporary block.

The concept of 'hybrid' procedure was first published by Pak et al.,[66] who combined percutaneous epicardial catheter ablation and endocardial ablation in difficult cases of AF. More recently, Krul et al.[47] presented their experience with thoracoscopic PV isolation and GP ablation guided by periprocedural electrophysiological testing. Mahapatra et al.[67] have recently published their initial experience with surgical epicardial-catheter and endocardial ablation for persistent and LSP atrial fibrillation carried out in two sequential steps (during the same hospitalization). After a mean follow-up of 20.7+4.5 months, 86.7% patients (persistent and LSP) were free of any atrial arrhythmia and off AADs, compared with 56.7% of patients undergoing repeat catheter ablation. More recently, Pison et al.[68] published results of a one-step hybrid thoracoscopic surgical and transvenous catheter ablation of atrial fibrillation in 26 patients. One-year off-AAD success free of AF/AFL/AT was 93% for patients with paroxysmal AF and 90% for patients with persistent AF. Nevertheless, demonstration of the effectiveness and the safety of this approach awaits the completion of studies currently underway. Figure 1 shows the conversion of AF to sinus rhythm during the one-step hybrid procedure.

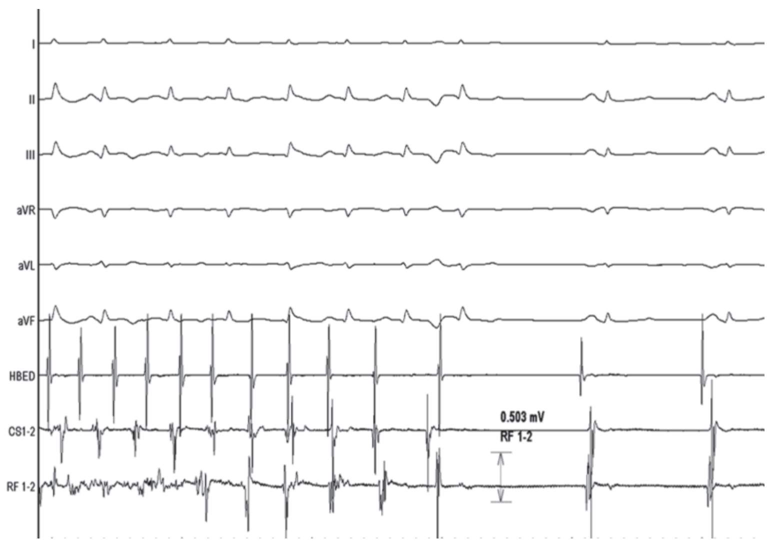


Figure 1. Hybrid procedure: conversion to sinus rhythm during epicardial ablation of the right superior ganglionated plexi (GP).

Limitations

This review has some important limitations which must be pointed out. First of all, a meta-analysis could not be carried out because of the heterogeneity of the papers and the lack of IPD. Second, the unavailability of data from prospective randomized studies on the minimally invasive surgical treatment of SA-AF vs. PCA was a drawback of this systemic review. Third, not all results are reported following HRS/EHRA/ECAS expert consensus which makes a comparison of the different studies difficult.

Conclusions

Minimally invasive surgical ablation of SA-AF achieved satisfactory 1-year results when the bipolar radiofrequency was employed as energy source with AAD-free success rate comparable to PCA. The success rate in paroxysmal was even higher than in PCA. In persistent and LSP, results were improved by additional LA ablation lines. In contrast, GP ablation and LAA removal seem not to influence the recurrence of AF and the occurrence of postoperative thromboembolic events. Nevertheless, the relatively high complication rate reported suggests that such techniques require further refinement. Finally, the preliminary results of the hybrid approach are promising but they need to be confirmed.

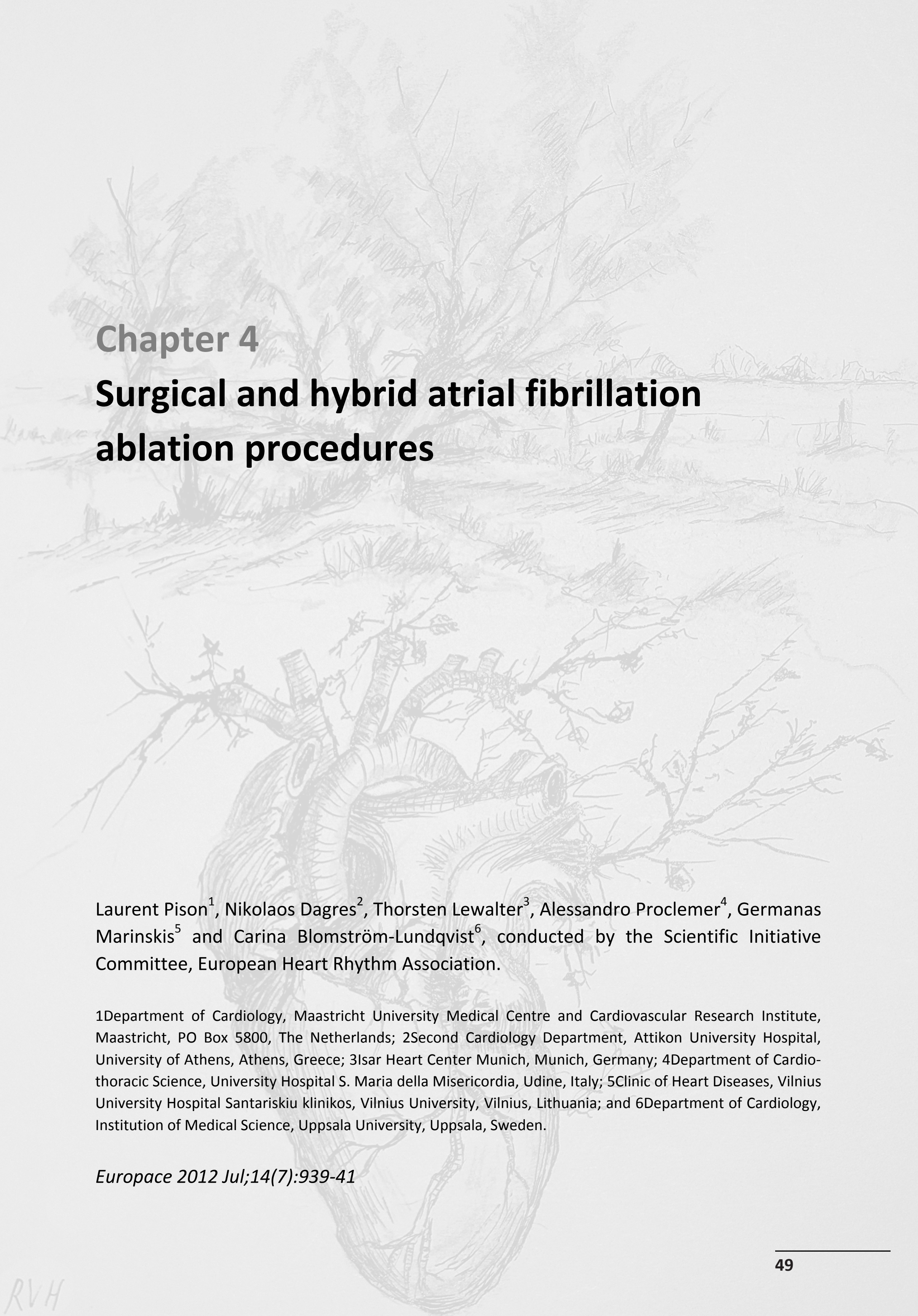
References

1. McCarthy PM, Gillinov AM, Castle L, Chung M, Cosgrove D III. The Cox-Maze procedure: the Cleveland Clinic experience. Semin Thorac Cardiovasc Surg 2000;12:25–9.
2. Prasad SM, Maniar HS, Camillo CJ, Schuessler RB, Boineau JP, Sundt TM III et al. The Cox maze III procedure for atrial fibrillation: long-term efficacy in patients undergoing lone versus concomitant procedures. J Thorac Cardiovasc Surg 2003;126:1822–8.
3. Pappone C, Santinelli V. Atrial fibrillation ablation: state of the art. Am J Cardiol 2005;96:59L–64L.
4. Calkins H, Brugada J, Packer DL, Cappato R, Chen SA, Crijns HJ et al. HRS/EHRA/ ECAS expert Consensus Statement on catheter and surgical ablation of atrial fibrillation: recommendations for personnel, policy, procedures and follow-up. A report of the Heart Rhythm Society (HRS) Task Force on catheter and surgical ablation of atrial fibrillation. Europace 2007;9:335–79.
5. Jais P, Hocini M, Sanders P, Hsu LF, Takahashi Y, Rotter M et al. Long-term evaluation of atrial fibrillation ablation guided by noninducibility. Heart Rhythm 2006;3:140–5.
6. Cappato R, Calkins H, Chen SA, Davies W, Iesaka Y, Kalman J et al. Worldwide survey on the methods, efficacy and safety of catheter ablation for human atrial fibrillation. Circulation 2005;111:1100–05.
7. Cappato R, Calkins H, Chen SA, Davies W, Iesaka Y, Kalman J et al. Updated worldwide survey on the methods, efficacy, and safety of catheter ablation for human atrial fibrillation. Circ Arrhythm Electrophysiol 2010;3:32–8.
8. Lall SC, Damiano RJ Jr. Surgical ablation devices for atrial fibrillation. J Interv Card Electrophysiol 2007;20:73–82.
9. Lee AM, Melby SJ, Damiano RJ Jr. The surgical treatment of atrial fibrillation. Surg Clin N Am 2009;89:1001–20.
10. Damiano RJ Jr. Surgical ablation of lone atrial fibrillation on the beating heart: the chaos continues. Europace 2010;12:297–8.
11. Gerosa G, Bianco R, Buja G, di Marco F. Totally endoscopic robotic-guided pulmonary vein ablation: an alternative method for the treatment of atrial fibrillation. Eur J Cardiothorac Surg 2004;26:450–2.
12. Balkhy HH, Chapman PD, Arnsdorf SE. Minimally invasive atrial fibrillation ablation combined with a new technique for thoracoscopic stapling of the left atrial appendage: case report. Heart Surg Forum 2004;7:353–5.
13. Poa L. Thoracoscopic ablation for treatment of atrial fibrillation: a 2-port approach. Heart Surg Forum 2006;9:e590–1.
14. La Meir M, De Roy L, Blommaert D, Buche M. Treatment of lone atrial fibrillation with a right thoracoscopic approach. Ann Thorac Surg 2007;83:2244–5.
15. Loulmet DF, Patel NC, Patel NU, Frumkin WI, Santoni-Rugiu F, Langan MN et al. First robotic endoscopic epicardial isolation of the pulmonary veins with microwave energy in a patient in chronic atrial fibrillation. Ann Thorac Surg 2004;78:e24–5.
16. Charokopos N, Rouska E, Styliadis I, Antonitsis P, Papakonstantinou C, Spanos P. Totally endoscopic microwave ablation for lone atrial fibrillation: an alternative method of treatment. Hell J Cardiol 2006;47:377–80.
17. Puskas J, Lin E, Bailey D, Guyton R. Thoracoscopic radiofrequency pulmonary vein isolation and atrial appendage occlusion. Ann Thorac Surg 2007;83:1870–2.
18. Li H, Li Y, Sun L, Liu X, Xu C, Han J et al. Minimally invasive surgical pulmonary vein isolation alone for persistent atrial fibrillation: preliminary results of epicardial atrial electrogram analysis. Ann Thorac Surg 2008;86:1219–25.
19. Jansens JL, Ducart A, Preumont N, Jottrand M, Stefanidis C, Stoupel E et al. Pulmonary vein isolation by robotic-enhanced thoracoscopy for symptomatic paroxysmal atrial fibrillation. Heart Surg Forum 2004;7:E595–8.
20. Grandmougin D, Tiffet O. Video-assisted thoracoscopic epicardial ablation of left pulmonary veins for lone permanent atrial fibrillation. Interact Cardiovasc Thorac Surg 2007;6:136–8.

21. Lee AM, Clark K, Bailey MS, Aziz A, Schuessler RB, Damiano RJ Jr. A minimally invasive Cox-Maze procedure: operative technique and results. Innovations (Phila) 2010;5:281–6.
22. Moten SC, Rodriguez E, Cook RC, Nifong LW, Chitwood WR Jr. New ablation techniques for atrial fibrillation and the minimally invasive cryo-maze procedure in patients with lone atrial fibrillation. Heart Lung Circ 2007;16(Suppl 3):S88–93.
23. Salenger R, Lahey SJ, Saltman AE. The completely endoscopic treatment of atrial fibrillation: report on the first 14 patients with early results. Heart Surg Forum 2004;7:E555-8.
24. Wolf RK, Schneeberger EW, Osterday R, Miller D, Merrill W, Flege JB Jr et al. Video-assisted bilateral pulmonary vein isolation and left atrial appendage exclusion for atrial fibrillation. J Thorac Cardiovasc Surg 2005;130:797–802.
25. Pruitt JC, Lazzara RR, Dworkin GH, Badhwar V, Kuma C, Ebra G. Totally endoscopic ablation of lone atrial fibrillation: initial clinical experience. Ann Thorac Surg 2006;81:1325–30.
26. Edgerton JR, Jackman WM. Minimally invasive pulmonary vein isolation and partial autonomic denervation for surgical treatment of atrial fibrillation. J Interv Card Electrophysiol 2007;20:89–93.
27. McClelland JH, Duke D, Reddy R. Preliminary results of a limited thoracotomy: new approach to treat atrial fibrillation. J Cardiovasc Electrophysiol 2007;18:1289–95.
28. Koistinen J, Valtonen M, Savola J, Airaksinen J. Thoracoscopic microwave ablation of atrial fibrillation. Interact Cardiovasc Thorac Surg 2007;6:695–8.
29. Pruitt JC, Lazzara RR, Ebra G. Minimally invasive surgical ablation of atrial fibrillation: the thoracoscopic box lesion approach. J Interv Card Electrophysiol 2007;20:83–7.
30. Sagbas E, Akpinar B, Sanisoglu I, Caynak B, Tamtekin B, Oral K et al. Video-assisted bilateral epicardial pulmonary vein isolation for the treatment of lone atrial fibrillation. Ann Thorac Surg 2007;83:1724–30.
31. Edgerton JR, Edgerton ZJ, Weaver T, Reed K, Prince S, Herbert MA et al. Minimally invasive pulmonary vein isolation and partial autonomic denervation for surgical treatment of atrial fibrillation. Ann Thorac Surg 2008;86:35–8.
32. Sirak J, Jones D, Sun B, Sai-Sudhakar C, Crestanello J, Firstenberg M. Toward a definitive, totally thoracoscopic procedure for atrial fibrillation. Ann Thorac Surg 2008;86:1960–4.
33. Wudel JH, Chaudhuri P, Hiller JJ. Video-assisted epicardial ablation and left atrial appendage exclusion for atrial fibrillation: extended follow-up. Ann Thorac Surg 2008;85:34–8.
34. Bagge L, Blomström P, Nillsson L, Einarsson GM, Jideus L, Blomström-Lundqvist C. Epicardial off-pump pulmonary vein isolation and vagal denervation improve long-term outcome and quality of life in patients with atrial fibrillation. J Thorac Cardiovasc Surg 2009;137:1265–71.
35. Beyer E, Lee R, Lam BK. Point: minimally invasive bipolar radiofrequency ablation of lone atrial fibrillation: early multicenter results. J. Thorac Cardiovasc Surg 2009;137:521–6.
36. Edgerton JR, McClelland JH, Duke D, Gerdisch MW, Steinberg BM, Bronleewe SH et al. Minimally invasive surgical ablation of atrial fibrillation: six-month results. J Thorac Cardiovasc Surg 2009;138:109–13.
37. Edgerton RJ, Jackman WM, Mahoney C, Mack MJ. Totally thoracoscopic surgical ablation of persistent atrial fibrillation and long-standing persistent atrial fibrillation using the 'Dallas' lesion set. Heart Rhythm 2009;6:S64–70.
38. Han FT, Kasirajan V, Kowalski M, Kiser R, Wolfe L, Kalahasty G et al. Results of a minimally invasive surgical pulmonary vein isolation and ganglionic plexi ablation for atrial fibrillation: single-center experience with 12-month follow-up. Circ Arrhythm Electrophysiol 2009;2:370–7.
39. Klinkenberg TJ, Ahmed S, Ten Hagen A, Wiesfeld AC, Tan ES, Zijlstra F et al. Feasibility and outcome of epicardial pulmonary vein isolation for lone atrial fibrillation using minimal invasive surgery and high intensity focused ultrasound. Europace 2009;11:1624–31.
40. Castella´ M, Pereda D, Mestres CA, Go´mez F, Quintana E, Mulet J. Thoracoscopic pulmonary vein isolation in patients with atrial fibrillation and failed percutaneous ablation. J Thorac Cardiovasc Surg 2010;140:633–8.
41. Cui YQ, Li Y, Gao F, Xu CL, Han J, ZengWet al. Video-assisted minimally invasive surgery for lone atrial fibrillation: a clinical report of 81 cases. J Thorac Cardiovasc Surg 2010;139:326–32.

42. Edgerton JR, Brinkman WT, Weaver T, Prince SL, Culica D, Herbert MA et al. Pulmonary vein isolation and autonomic denervation for the management of paroxysmal atrial fibrillation by a minimally invasive surgical approach. J Thorac Cardiovasc Surg 2010;140:823–8.
43. Sirak J, Jones D, Schwartzman D. The five-box thoracoscopic maze procedure. Ann Thorac Surg 2010;90:986–9.
44. Speziale G, Bonifazi R, Nasso G, Bartolomucci F, Caldarola P, Fattouch K et al. Minimally invasive radiofrequency ablation of lone atrial fibrillation by monolateral right minithoracotomy: operative and early follow-up results. Ann Thorac Surg 2010;90:161–7.
45. Stamou SC, Khabbaz KR, Mahmood F, Zimetbaum P, Hagberg RC. A multidisciplinary approach to the minimally invasive pulmonary vein isolation for treatment of atrial fibrillation. Ann Thorac Surg 2010;89:648–50. 221.
46. Yilmaz A, Geuzebroek GS, Van Putte BP, Boersma LV, Sonker U, De Bakker JM et al. Completely thoracoscopic pulmonary vein isolation with ganglionic plexus ablation and left atrial appendage amputation for treatment of atrial fibrillation. Eur J Cardiothorac Surg 2010;38:356–60.
47. Krul SP, Driessen AH, van Boven WJ, Linnenbank AC, Geuzebroek GS, Jackman WM et al. Thoracoscopic video-assisted pulmonary vein antrum isolation, ganglionated plexus ablation, and periprocedural confirmation of ablation lesions: first results of a hybrid surgical-electrophysiological approach for atrial fibrillation. Circ Arrhythm Electrophysiol 2011;4:262–70.
48. La Meir M, Gelsomino S, Luca F, Pison L, Chambille P, Parise O et al. Time-related prevalence of postoperative atrial fibrillation after stand-alone minimally invasive radiofrequency ablation. J Card Surg 2011;26:453–9.
49. Nasso G, Bonifazi R, Del Prete A, Del Prete G, Lopriore V, Bartolomucci F et al. Long-term results of ablation for isolated atrial fibrillation through a right minithoracotomy: toward a rational revision of treatment protocols. J Thorac Cardiovasc Surg 2011;142:e41–6.
50. Wang JG, Li Y, Shi JH, Han J, Cui YQ, Luo TG et al. Treatment of long-lasting persistent atrial fibrillation using minimally invasive surgery combined with irbesartan. Ann Thorac Surg 1011;91:1183–90.
51. Chambers PW. Lone atrial fibrillation: pathologic or not? Med Hypotheses 2007;68:281–7.
52. Fuster V, Ryde´n LE, Cannom DS, Crijns HJ, Curtis AB, Ellenbogen KA et al. ACC/AHA/ESC 2006 guidelines for the management of patients with atrial fibrillation: full text. Europace 2006;8:651–754.
53. Lévy S, Camm AJ, Saksena S, Aliot E, Breithardt G, Crijns H et al. Working group on Arrhythmias, Working group on Cardiac Pacing of the European Society of Cardiology, North American Society of Pacing and Electrophysiology. International consensus on nomenclature and classification of atrial fibrillation; a collaborative project of the Working group on Arrhythmias and the Working group on Cardiac Pacing of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology. Europace 2003;5:119–22.
54. Camm AJ, Kirchhof P, Lip GY, Schotten U, Savelieva I, Ernst S et al. Guidelines for the management of atrial fibrillation: the Task Force for the Management of Atrial Fibrillation of the European Society of Cardiology (ESC). Europace 2010;12:1360–420.
55. Shemin RJ, Cox JL, Gillinov AM, Blackstone EH, Bridges CR. Workforce on Evidence-Based Surgery of the Society of Thoracic Surgeons. Workforce on Evidence-Based Surgery of the Society of Thoracic Surgeons. Guidelines for reporting data and outcomes for the surgical treatment of atrial fibrillation. Ann Thorac Surg 2007;83:1225–30.
56. Prasad SM, Maniar HS, Schuessler RB, Damiano RJ Jr. Chronic transmural atrial ablation by using bipolar radiofrequency energy on the beating heart. J Thorac Cardiovasc Surg 2002;124:708–13.
57. Weerasooriya R, Khairy P, Litalien J, Macle L, Hocini M, Sacher F et al. Catheter ablation for atrial fibrillation: are results maintained at 5 years of follow-up? J Am Coll Cardiol 2011;57:160–6.
58. Mounsey JP. Recovery from vagal denervation and atrial fibrillation inducibility: effects are complex and not always predictable. Heart Rhythm 2006;3:709–10.
59. Roy D, Talajic M, Dorian P, Connolly S, Eisenberg MJ, Green M et al. Amiodarone to prevent recurrence of atrial fibrillation. Canadian Trial of Atrial Fibrillation Investigators. N Engl J Med 2000;342:913–20.

60. Gelsomino S, La Meir M, Luca` F, Lorusso R, Crudeli E, Vasquez L et al. Treatment of lone atrial fibrillation: a look at the past, a view of the present and a glance at the future. Eur J Cardiothorac Surg 2012. doi:10.1093/ejcts/ezr222.
61. Krul SP, Driessen AH, Zwinderman AH, van Boven WJ, Wilde AA, de Bakker JM et al. Navigating the mini-maze: Systematic review of the first results and progress of minimally-invasive surgery in the treatment of atrial fibrillation. Int J Cardiol 2011. doi:10.1016/j.ijcard.2011.10.011.
62. Walker E, Hernandez AV, Kattan MW. Meta-analysis its strength and limitations. Clev Clin J Med 2008;75:431–9.
63. Lyman GH, Kuderer NM. The strengths and limitations of meta-analyses based on aggregate data. BMC Med Res Method 2005;5:14.
64. Shinbane JS, Lesh MD, Stevenson WG, Klitzner TS, Natterson PD, Wiener I et al. Anatomic and electrophysiologic relation between the coronary sinus and mitral annulus: implications for ablation of left-sided accessory pathways. Am Heart J 1998;135:93–8.
65. Sauren LD, La Meir M, De Roy L, Pison L, van der Veen FH, Mess WH et al. Increased number of cerebral emboli during percutaneous endocardial pulmonary vein isolation versus a thoracoscopic epicardial approach. Eur J Cardiothorac Surg 2009;36:833–7.
66. Pak HN, Hwang C, Lim HE, Kim JS, Kim YH. Hybrid epicardial and endocardial ablation of persistent or permanent atrial fibrillation: a new approach for difficult cases. J Cardiovasc Electrophysiol 2007;18:917–23.
67. Mahapatra S, LaPar DJ, Kamath S, Payne J, Bilchick KC, Mangrum JM et al. Initial experience of sequential surgical epicardial-catheter endocardial ablation for persistent and long-standing persistent atrial fibrillation with long-term follow-up. Ann Thorac Surg 2011;91:1890–8.
68. Pison L, La Meir M, van Opstal J, Blaauw Y, Maessen JG, Crijns HJ. Hybrid thoracoscopic surgical and transvenous catheter ablation of atrial fibrillation. J Am Coll Cardiol 2012;60:54–61.



Chapter 4

Surgical and hybrid atrial fibrillation ablation procedures

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Abstract

Aims

The purpose of this EP Wire is to survey clinical practice in this rapidly evolving field as the variety of surgical techniques and the heterogeneity of treated patients make the comparison of results and outcomes challenging.

Methods

Twenty-four European centres, all members of the EHRA EP research network, responded to this survey and completed the questions.

Results

Of the participating centres, 11 (46%) performed (irrespective of the technique) stand-alone surgical AF ablation in 2011. Seven hospitals (64%) perform totally thoracoscopic AF ablation procedures off-pump (in 20% to 100% of their cases). The most commonly used lesion set was pulmonary vein isolation (PVI) only in 5 hospitals (46%). Eight centres (73%) performed validation of the surgical lesion set at the time of intervention. The most important indication for performing stand-alone, totally thoracoscopic surgical AF ablation in 7 participating hospitals, was failed catheter ablation. According to their definition of success, participating centres reported their success rate to be 10% to 100% for paroxysmal AF and 0% to 95% for (longstanding) persistent AF. The most frequently encountered complications during stand alone, surgical AF ablation, were pneumothorax and haemothorax in up to 10% of the cases.

Conclusion

This EP Wire survey shows a wide variation not only in indications for stand-alone, surgical AF ablation, but also in surgical techniques, lesion sets, follow-up and outcome.

Introduction

Surgical techniques for curative ablation of atrial fibrillation (AF), have evolved from the original cut-and-sew Cox Maze-III procedure to minimally invasive stand alone procedures with new energy sources and electrophysiological validation of the lesion set which requires close collaboration between cardiologists and cardiac surgeons.[1-4]

The purpose of this EP Wire is to survey clinical practice in this rapidly evolving field as the variety of surgical techniques and the heterogeneity of treated patients make the comparison of results and outcomes challenging.

Results

Twenty-four European centres, all members of the EHRA EP research network, responded to this survey and completed the questionnaires. Nineteen of them were university hospitals (79%), 2 non-university and 3 private hospitals. The total number of endocardial catheter based AF ablations performed in 2011, was less than 50 procedures in 10 centres (42%), 50 to 99 procedures in 7 centres (29%), 100 to 199 procedures in 5 centres (21%) and 200 or more procedures in 2 centres (8%). Only 3 centres (12,5%) indicated that more than 30% of these transcatheter AF ablations were performed in patients with (longstanding) persistent AF. Four of the responding centres (16,7%) didn't have onsite cardiac surgery.

Of the participating centres, 11 (46%) performed (irrespective of the technique) stand-alone surgical AF ablation in 2011: 6 centres less than 50 procedures, 4 centres between 50 and 99, 1 centre more than 100.

Three of these centres indicated that they apply the Cox Maze on-pump technique using radiofrequency (RF) or cryoablation to create linear lesions in 100% of the cases. Seven hospitals perform totally thoracoscopic AF ablation procedures off-pump (in 20% to 100% of their cases). The original cut-and-sew Cox Maze-III procedure is still used in 3 centres (from 1% to 10% of their procedures). The minimally invasive Cox Maze-IV procedure is used in two hospitals and the simultaneous totally thoracoscopic epicardial and transvenous endocardial AF ablation in one.

In 5 hospitals the most commonly used lesion set was pulmonary vein isolation (PVI) only. Three centres applied PVI in combination with a box lesion (roof and inferior line) and 2 centres PVI with the Cox Maze-III linear lesion set only on the left atrium. Just one centre used PVI with the Cox Maze-III linear lesion set on both atria. Only two centres performed off-pump PVI with a box lesion and ablation of complex fractionated atrial electrograms (CFAE). The combination of PVI, box lesion and left atrial appendage (LAA) line was done in 2 centres.

Eight centres (73%) performed validation of the surgical lesion set at the time of intervention, that is, checked conduction block of the pulmonary veins and bidirectional block across linear lesions. In three centres this was done epicardially and endocardially.

Among the 6 centres performing mostly off-pump stand-alone surgical AF ablation (i.e. at least 90% of the procedures are totally thoracoscopic epicardial ablations or simultaneous totally thoracoscopic epicardial and transvenous endocardial ablations), the LAA was always removed (stapling) or closed (epicardial clip) during this procedure in 3 of them (50%). One hospital (17%) never removed or closed the LAA and the remaining 2 centres (33%) only did so when the CHA2DS2-VASC score was ≥ 2.

Nine hospitals (82%) used exclusively RF during their stand-alone AF ablation procedures. One centre used only cryoenergy and another one a combination of microwave and RF.

The most important indication for performing stand-alone, totally thoracoscopic surgical AF ablation in 7 participating hospitals, was failed catheter ablation (Figure 1). The other indications were (in descending order of importance) primary intervention for longstanding persistent AF, patient preference, thrombo-embolic advantage with LAA exclusion, shorter waiting list, failed transseptal technique and study protocol.

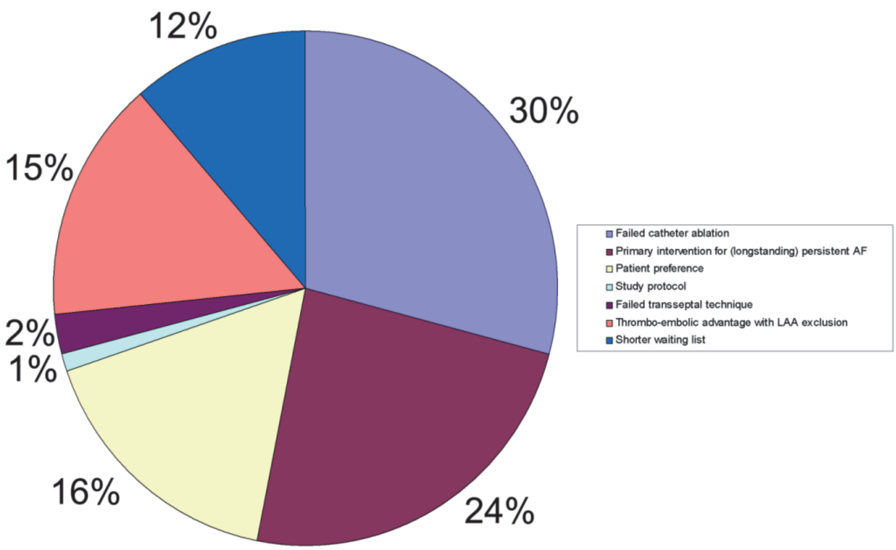

Figure 1. Indications for stand alone, surgical atrial fibrillation ablation.
AF = atrial fibrillation, LAA = left atrial appendage.

Nine of the eleven centres performing stand-alone surgical AF ablation, reported how they perform monitoring after surgery. Two hospitals planned sporadic 24 hours Holter, two relied on implantable loop recorders, two performed 7 days Holter at 3,6,9 and 12 months post procedure, two monitored their patients clinically only depending on symptoms and one centre used telemetry.

Successful therapy was defined as absence of symptoms and complete absence of AF defined as episodes lasting more than 30 seconds, in 7 centres (64%). One centre defined success as absence of AF and one as significant reduction of AF burden. Two centres didn't disclose on their definition of a successful therapy.

According to their definition of success, participating centres reported their success rate to be 10% to 100% for paroxysmal AF and 0% to 95% for (longstanding) persistent AF.

The most frequently encountered complications during stand alone, surgical AF ablation, were pneumothorax and haemothorax in up to 10% of the cases. The majority of those pneumothoraces were postoperative findings on X-ray without clinical consequences. Participating hospitals mentioned also tamponade (1-2%), TIA/stroke (1-5%), rib fracture (2%), sternotomy for bleeding (1-5%), pneumonia (3-4%) and pacemaker implantation (1%). Six centres reported to have no complications during their most commonly performed stand-alone, surgical AF ablation procedure.

The percentage of atrial tachycardia (excluding cavotricuspid isthmus-dependent atrial flutter) after surgical AF ablation, ranged from 10% to 40%.

Discussion

In this EP Wire survey, we have shown that stand-alone, surgical AF ablation is not yet widely applied and mainly indicated after failed catheter ablation. Several surgical techniques and lesion sets are used for this purpose and there is a great variance in success rates.

For more than two decades, the cut-and-sew Cox Maze-III procedure was the gold standard for the surgical treatment of AF and has proven to be effective at eliminating this arrhythmia. Despite its proven efficacy, the Cox Maze-III procedure did not gain widespread acceptance owing to its complexity and technical difficulty.[1] To simplify the procedure, groups have replaced the incisions of the Cox Maze-III with linear lines of ablation.[5-8] The introduction of new ablation technologies using among others RF energy and cryoablation, have been used as alternatives to the cut-and-sew surgical treatment of AF with the ultimate goal to perform a curative lesion set epicardially on the beating heart, without the need for cardiopulmonary bypass. This is also reflected in this survey: only a minority of responding centres still use the cut-and-sew Cox Maze-III procedure. Most centres perform less invasive procedures as the totally thoracoscopic AF ablation procedures off pump, the minimally invasive Cox Maze-IV procedure or the simultaneous totally thoracoscopic epicardial and transvenous endocardial AF ablation.

Although PVI remains essential for most catheter and surgical ablation procedures, the role of substrate modification has taken on increasing importance.9 The majority of hospitals participating in this survey, perform PVI in combination with substrate modification which can be the creation of linear lesions and/or ablation of CFAEs. To minimize the risk of reconnection after PVI and the occurrence of macroreentry circuits due to incomplete linear lesions, more than 70% of centres do perform validation of the surgical lesions set. It is not clear from the results of this survey, whether the type of AF influenced the technique or lesion set that was used.

According to the latest European guidelines for the management of AF, minimally invasive surgical ablation of AF without concomitant cardiac surgery may be performed in patients with symptomatic AF after failure of catheter ablation (class of recommendation IIb, level of evidence C).10 The results of this survey confirm that this is the case in clinical practice among participating centres as failure of catheter ablation is the most important indication for stand alone, surgical AF ablation.

In the consensus statement of 2007, it was recommended to perform a 24-hour Holter monitoring at 3- to 6-month intervals for 1–2 years after catheter AF ablation.[11] Clinical practice seems to be quite different: two centres adhere to this guideline but the others use implantable loop recorders, 24-hour Holter sporadically or only symptom triggered monitoring. On the other hand, however, the majority of centres define success according to current guidelines: absence of symptoms and complete absence of AF defined as episodes lasting more than 30 seconds. The success rates of stand alone, surgical AF ablation among participating centres are very disparate: ranging from 10% to 100% for paroxysmal AF and 0% to 95% for (longstanding) persistent AF. Nevertheless, it remains difficult to compare results given the fact that different techniques and lesion sets are used and the non-uniformity in monitoring of the patients. The authors do believe that those findings should prompt the initiation of prospective registries and trials, in order to standardize these procedures and hence make it possible to compare procedural data and outcomes.

The complication rate revealed in this survey was comparable with the recently published FAST trial data.[12] Pneumothorax and haemothorax were the most frequent complications in up to 10% of the procedures.

Conclusions

This EP Wire survey shows a wide variation not only in indications for stand-alone, surgical AF ablation, but also in surgical techniques, lesion sets, follow-up and outcome.

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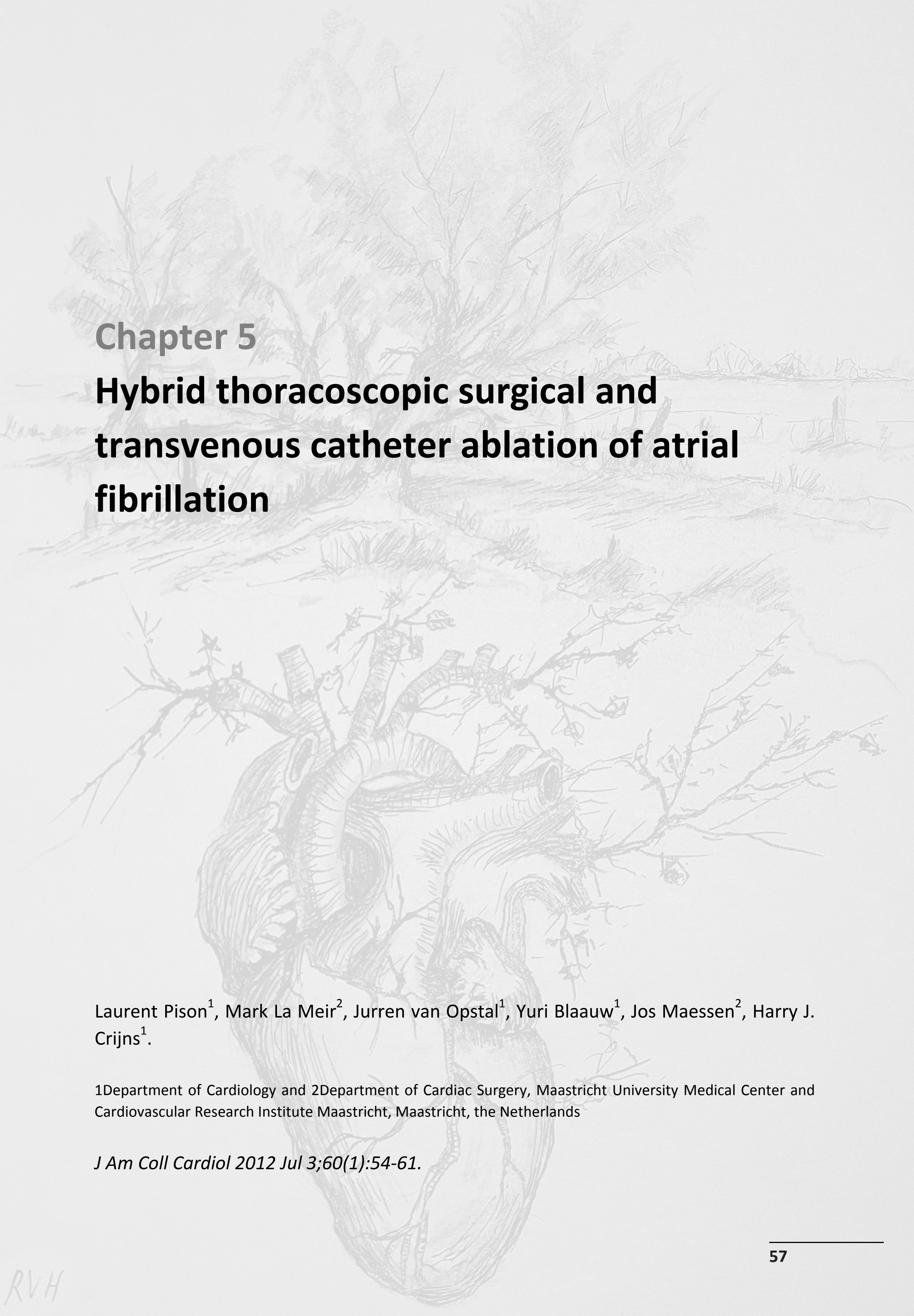
References

1. Lönnerholm S, Blomström P, Nilsson L, Oxelbark S, Jideus L, Blomström-Lundqvist C. Effects of the maze operation on health-related quality of life in patients with atrial fibrillation. *Circulation* 2000 Jun 6;101:2607-11.
2. Wolf RK, Schneeberger EW, Osterday R, Miller D, Merrill W, Flege JB, et al. Video-assisted bilateral pulmonary vein isolation and left atrial appendage exclusion for atrial fibrillation. *J Thorac Cardiovasc Surg* 2005;130:797-802.
3. Krul SP, Driessen AH, van Boven WJ, Linnenbank AC, Geuzebroek GS, Jackman WM, et al. Thoracoscopic video-assisted pulmonary vein antrum isolation, ganglionated plexus ablation, and periprocedural confirmation of ablation lesions. *Circ Arrhythm Electrophysiol* 2011;4:262-270.
4. Pison L, La Meir M, van Opstal J, Blaauw Y, Maessen J, Crijns HJ. Hybrid thoracoscopic surgical and transvenous catheter ablation of atrial fibrillation. *J Am Coll Cardiol*, in press, doi:10.1016/j.jacc.2011.12.055.
5. Khargi K, Hutten BA, Lemke B, Deneke T. Surgical treatment of atrial fibrillation: a systematic review. *Eur J Cardio-thorac Surg* 2005;27:258 –265.
6. Damiano RJ Jr. Alternative energy sources for atrial ablation: judging the new technology. Invited editorial. *Ann Thorac Surg* 2003;75:329 –330.
7. Shen J, Bailey MS, Damiano RJ. The surgical treatment of atrial fibrillation. *Heart Rhythm* 2009;6:S45–S50.
8. Bagge L, Blomström P, Nilsson L, Einarsson GM, Jidéus L, Blomström-Lundqvist C. Epicardial off-pump pulmonary vein isolation and vagal denervation improve long-term outcome and quality of life in patients with atrial fibrillation. *J Thorac Cardiovasc Surg* 2009;137:1265-71.
9. Katritsis D, Merchant FM, Mela T, Singh JP, Heist EK, Armoundas AA. Catheter ablation of atrial fibrillation. The Search for Substrate-Driven End Points. *J Am Coll Cardiol* 2010;55:2293–8.
10. Camm AJ, Kirchhof P, Lip GYH, Schotten U, Savelieva I, Ernst S, et al. Guidelines for the Management of Atrial Fibrillation. The Task Force for the Management of Atrial Fibrillation of the European Society of Cardiology (ESC). *Eur Heart J* 2010;31:2369-2429.
11. Calkins H, Brugada J, Packer DL, Cappato R, Chen SA, Crijns HJ, et al. HRS/EHRA/ECAS expert consensus statement on catheter and surgical ablation of atrial fibrillation: recommendations for personnel, policy, procedures, and follow-up: a report of the Heart Rhythm Society Task Force on Catheter and Surgical Ablation of Atrial Fibrillation. *Heart Rhythm* 2007;4:816–861.
12. Boersma LV, Castella M, van Boven WJ, Berruezo A, Yilmaz A, Nadal M, et al. Atrial Fibrillation Catheter Ablation Versus Surgical Ablation Treatment (FAST). A 2-Center Randomized Clinical Trial. *Circulation* 2012;125:23-30.



Chapter 5

Hybrid thoracoscopic surgical and transvenous catheter ablation of atrial fibrillation

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Abstract

Objectives

The purpose of this study was to evaluate the feasibility, safety, and clinical outcome up to 1 year for patients undergoing a combined simultaneous thoracoscopic surgical and transvenous catheter atrial fibrillation (AF) ablation.

Background

The combination of the transvenous endocardial approach with the thoracoscopic epicardial approach in a single AF ablation procedure, overcomes the limitations of both techniques and should result in better outcomes.

Methods

We followed a cohort of 26 consecutive patients with AF who underwent a hybrid thoracoscopic surgical and transvenous catheter ablation (CA) with a follow-up of up to 1 year.

Results

Twenty-six patients (42% persistent AF) underwent a successful hybrid procedure. There were no complications. Mean follow-up was 470±154 days. In 23% of the patients, the epicardial lesions were not transmural and endocardial touch-up was necessary. One-year success defined according to the Heart Rhythm Society/European Heart Rhythm Association/European Cardiac Arrhythmia Society consensus statement for the catheter and surgical ablation of AF, was 93% for patients with paroxysmal AF and 90% for patients with persistent AF. Two patients underwent CA for recurrent AF or left atrial flutter after the hybrid procedure.

Conclusions

A combined transvenous endocardial and thoracoscopic epicardial ablation procedure for AF, is a feasible and safe procedure with a single-procedure success rate of 83% at 1 year.

Introduction

In paroxysmal atrial fibrillation (AF), success rates of catheter ablation (CA) exceed 80% and recurrence is mostly associated with pulmonary vein (PV) reconnection (1,2). By combining PV isolation, complex and fractionated atrial electrogram ablation, and linear lesions in persistent AF patients, success rates without anti-arrhythmic drug (AAD) surpass 70% (3,4). However, multiple procedures are often necessary and creating linear lesions is sometimes challenging.

Surgical AF ablation has evolved from the original Cox-maze procedure towards a minimally invasive video-assisted procedure with new ablation tools to isolate the PVs and create linear lesions without opening the heart (5). Nevertheless, even bipolar radiofrequency (RF) energy cannot guarantee transmural lesions (6). Linear lesions such as the mitral isthmus, cannot be created solely from the epicardium, and proving bidirectional block epicardially, can be challenging (7).

Combining a transvenous endocardial and thoracoscopic epicardial approach in a single procedure, overcomes these shortcomings.

We report our initial experience with long term follow-up of minimally invasive epicardial bilateral PV isolation and linear lesions in combination with endocardial proof of conduction block and endocardial touch-up if indicated.

Methods

Patient selection

Twenty-six consecutive patients with symptomatic AF underwent a hybrid thoracoscopic surgical and transvenous CA with a follow-up of 1 year. Definitions of paroxysmal/persistent/longstanding persistent AF, success and failure of ablation, and follow-up monitoring were based on the Heart Rhythm Society/European Heart Rhythm Association/European Cardiac Arrhythmia Society consensus statement (3). Patients had failed at least 1 AAD. Other selection criteria were previously failed CA, left atrium (LA) volume ≥ 29ml/m^2, persistent or longstanding persistent AF, or patient preference for a hybrid procedure instead of a percutaneous approach. Eleven patients (44%) had a prior CA for AF or atrial flutter (AFL). All patients underwent transthoracic echocardiography, cardiac computed tomography, and pulmonary function test preoperatively.

Hybrid procedure

The procedure was performed under general anesthesia with double-lumen endotracheal tube placement for selective lung ventilation. Transoesophageal echocardiography was used to exclude a thrombus in the LA. On the right side, a 12 mm cameraport was placed in the 5th intercostal space mid axillary line and in the 6th or 7th intercostal space anterior axillary line. A 5 mm workingport was placed in the 3rd intercostal space anterior axillary line. The pericardium was opened anterior to the phrenic nerve. Blunt dissection was used to open the transverse and oblique sinuses.

Via femoral venous approach, a His bundle (St. Jude Medical, St. Paul, MN, USA) and coronary sinus catheter (Medtronic, Minneapolis, MN, USA) were placed under fluoroscopy and transseptal puncture was performed with a long sheath 8F (SL0, St. Jude Medical, St. Paul, MN, USA) into the LA. We then heparinised the patient (1000 units of heparin per 10 kilograms bodyweight and a heparin infusion) with activated clotting time above 300 seconds. During rapid ventricular pacing, we injected contrast through the long sheath to visualize LA anatomy. The PVs were mapped with a circular mapping catheter (Lasso, Biosense Webster, Diamond Bar, USA). Antral isolation of the right PVs as pair, was performed with 4 to 6 applications using a bipolar RF clamp (Atricure, West Chester, OH, USA) (Figure 1). Each application had a duration of about 15 seconds with a median output of 10 to 15 Watt. The same port incisions were made on the left side but placed more posteriorly (Figure 2). The pericardium was divided posterior to the phrenic nerve. Left PV isolation was conducted as described above. We did not attempt ablation of the ganglionated plexus.

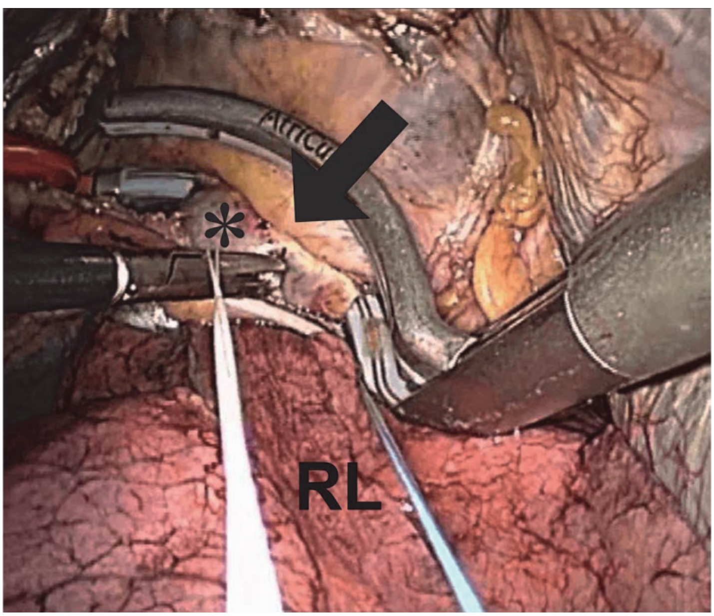


Figure 1. Right Pulmonary Vein Isolation
A large antral lesion (arrow) is created using a bipolar radiofrequency clamp and resulting in complete isolation of the right pulmonary veins (PV). The antrum of the right PVs is clearly visible (*). RL = right lung.

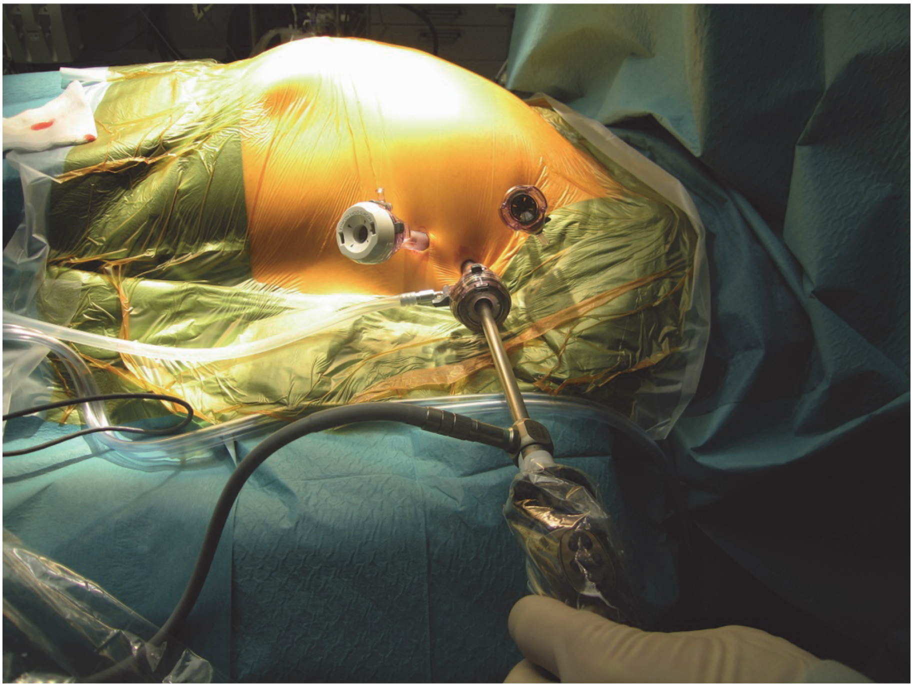


Figure 2. Placement of Ports on Left Side of the Patient

In patients with severe chronic obstructive pulmonary disease , we performed a thoracoscopic epicardial isolation of the PVs only on the right and the left PVs were isolated using a cryothermal energy balloon catheter (Arctic Front, Cryocath, Montreal, Quebec, Canada) endocardially to avoid bilateral sequential lung deflation.

The endpoint for PV ablation, was entrance and exit block. We defined exit block as local capture in the PV during pacing from the Lasso catheter (output 10mA, pulse width 2 ms) without conduction to the LA. In the case of sinus rhythm after PV isolation, reinduction of AF was attempted 5 times by pacing in the coronary sinus for 10 seconds at the shortest cycle length resulting in 1:1 atrial capture. AF was considered inducible if it lasted more than 1 minute. If AF became noninducible, isoproterenol was infused at rates of 10 to 30 µg/min. If AF had not terminated or still was inducible, linear lesions were deployed.

A roof line (connecting both superior PVs) and inferior line (connecting both inferior PVs) were made epicardially using a bipolar RF pen or linear pen device (Isolater Pen and Coolrail, Atricure, West Chester, OH, USA). If the right atrium was dilated, two additional ablation lines were placed: one encircling the superior caval vein using the clamp, the other connecting both caval veins using the pen.

By making a roof and inferior line, we isolated the posterior LA (box lesion). If entrance and exit block were not reached, we identified the conduction gaps endocardially and ablated those with a 3.5-mm-tip catheter (ThermoCool, Biosense Webster, Diamond Bar, USA). The location of the linear lesions was visualised with the linear pen device in situ and using fluoroscopy.

A left isthmus line was made in 3 patients using the bipolar RF pen device. The line was started from the ablation line on the antrum of the left inferior PV towards and crossing the coronary sinus. All patients needed an endocardial touch-up ablation to reach bidirectional block, starting from the mitral annulus towards or inside the coronary sinus. If the patient was known with typical AFL or if this arrhythmia occured during the procedure, the cavotricuspid isthmus (CTI) was ablated endocardially. The endpoint was bidirectional block. In 7 patients the LA appendage was removed using a stapling device.

The pericardium was approximated with a stitch, and a chest tube was placed in both pleural cavities. There was no drain left in the pericardial space.

Low molecular weight heparins were started six hours after the procedure and on the second postoperative day, acenocoumarol was reinitiated.

Patients restarted as soon as possible their pre-operative AAD regimen. Acenocoumarol and AADs were discontinued after the 6-month monitor confirmed the absence of atrial arrhythmia.

Long-term follow-Up

Any symptomatic patient not in sinus rhythm was cardioverted before the 3-month follow-up visit. One patient had a pacemaker, which was used for monitoring. The remaining patients underwent 7-days continuous Holter monitoring at 3, 6, 9, and 12 months. If 7-days Holter was not available, the patients underwent at least 24 hours Holter monitoring. According to current guidelines, success was defined as no episode of AF, AFL, or any atrial tachycardia (AT) lasting more than 30 seconds off AAD after the three months blanking period.

Statistical analysis

Data were retrospectively entered into a database. Statistical analysis was performed using SPSS 16.0. Continuous variables are summarized with means and standard deviations. Outcome is displayed with a Kaplan Meier plot and compared with a log-rank test. Any episode of AF, AFL, or AT lasting more than 30 seconds detected after the 3-month postprocedural period by ECG, pacemaker interrogation, or 7-days/48 hours/24 hours continuous Holter monitor performed at 6, 9, and 12 months, was considered as a failure.

Results

Perioperative results

Twenty-six patients underwent a hybrid procedure between May 29, 2008, to February 25, 2010. Patient baseline characteristics are shown in Table 1. Ten patients had persistent AF and 1 longstanding persistent AF. Eleven patients had 1 or 2 (patient 25) previous CAs. None of the PVs were isolated in those patients and there were no epicardial scars indicative of transmural lesions. Mean follow-up was 470±154 days (221 to 858 days). Mean length of hospital stay was 7±2 days (5 to 13 days) and mean ICU stay for postprocedural recovery was 1,0±0,2 days (1 to 2 days). The median length of the hybrid procedure (from initial skin incision to skin closure) was 280±84 minutes (195 to 505 minutes).

Eleven patients were in AF at the start of the procedure. In all patients we achieved bidirectional block of all the PVs (Figure 3). In 2 patients we did not perform any other lesion, because AF was not inducible. In 1 patient with inducible AF after PV isolation, we performed an additional roof line only. In 1 patient with inducible right AFL after PV isolation, we performed an additional CTI line only. Thereafter, no arrhythmia could be induced. In 22 patients we created a box lesion epicardially. In 17 patients (77%) we were able to demonstrate endocardial entrance and exit block in the box during sinus rhythm. After endocardial touch-up in 5 patients (23%), we completed the box lesion. In 3 patients there was a gap at the junction of the right superior PV with the roof of the LA. One patient had a gap in the lateral portion of the roof line and 1 patient in the middle of the inferiorline. Because of ongoing AF or organisation into a mitral isthmus dependent AFL, we performed in 3 patients a mitral isthmus line epicardially. In all cases, it had to be completed from the endocardium or coronary sinus with a mean of 1.6±0.5 applications of RF energy, resulting in bidirectional block (Figure 4). In 2 patients, a CTI ablation was performed. One patient needed electrical cardioversion at the end of the procedure due to ongoing AF. All the other patients were in sinus rhythm. Twenty-four (92%) patients were discharged on their pre-operative AAD regimen (amiodarone, 6/24; 25%). All patients were discharged on acenocoumarol.

Table 1. Baseline Characteristics

Patient	Age	Gender	EF	AF type	AF duration	LA vol/lpsa	BMI	Previous CA	Hypertension	CAD	CHADS2	COPD	Lesion set	Follow-up
1	70	M	63	Pers	12	133/51	24,2	No	Yes	Yes	1	No	PVI, box, mitral isthmus line	1 year: NSR without AAD
2	54	M	66	Pers	60	110/47	26,3	No	Yes	No	1	No	PVI, box, bicaval line, CTI	2 year: NSR without AAD
3	62	M	53	Pers	24	97/53	28,8	Yes	No	Yes	0	No	PVI, box	1 year: NSR without AAD
4	69	M	44	Pers	72	96/46	31	Yes	No	Yes	0	No	PVI, box, bicaval line, SCV	6 months: NSR with sotalol
5	52	M	43	Pers	36	95/46	24,5	No	No	No	1	No	PVI, box, bicaval line, SCV, ICV	1 year: NSR without AAD
6	53	F	63	Pers	156	88/42	27,7	Yes	No	Yes	0	No	PVI	1 year: AF with flecainide
7	50	M	57	Pers	84	86/44	28,3	Yes	No	No	0	No	PVI, box, bicaval line, SCV, ICV	1 year: NSR without AAD
8	48	F	49	Pers	36	83/40	22,9	No	No	No	0	No	PVI, box, mitral isthmus line	2 year: NSR without AAD
9	54	F	47	Pers	12	80/48	29,7	No	No	No	0	No	PVI, box, bicaval line, SCV, ICV	1 year: NSR without AAD
10	60	M	55	Pers	12	71/36	22,1	No	No	No	0	No	PVI, box	1 year: NSR without AAD
11	46	M	56	Pers	48	38/32	24,3	Yes	Yes	No	1	Yes	PVI, box, bicaval line, SCV	1 year: NSR without AAD
12	58	M	67	Parox	36	130/45	28,7	Yes	Yes	Yes	1	No	PVI, box	1 year: NSR after redo CA LA flutter
13	70	M	63	Parox	36	111/42	23,8	No	Yes	Yes	1	No	PVI, box	1 year: NSR without AAD
14	62	F	61	Parox	36	110/45	26,2	No	No	Yes	0	No	PVI, box	1 year: NSR without AAD
15	57	M	62	Parox	24	99/45	30,9	No	Yes	No	1	No	PVI, box	1 year: AF with sotalol
16	60	M	62	Parox	108	90/48	28,1	No	Yes	Yes	1	Yes	PVI, box	1 year: NSR without AAD

Patient	Age	Gender	EF	AF type	AF duration	LA vol/lpsa	BMI	Previous CA	Hypertension	CAD	CHADS2	COPD	Lesion set	Follow-up
17	66	M	57	Parox	120	84/45	23,5	No	Yes	Yes	1	Yes	PVI, box	1 year: NSR after redo CA right PVs and roofline
18	62	M	67	Parox	156	84/46	26,9	No	Yes	No	1	No	PVI	1 year: NSR without AAD
19	66	M	63	Parox	108	82/44	32,2	Yes	Yes	No	1	No	PVI, CTI line	1 year: NSR without AAD
20	48	M	63	Parox	120	94/43	31,6	Yes	No	No	0	No	PVI, box	1 year: NSR without AAD
21	59	M	70	Parox	120	80/45	26,1	No	Yes	Yes	1	Yes	PVI, box	1 year: NSR without AAD
22	62	F	66	Parox	72	76/49	35,6	No	Yes	Yes	1	Yes	PVI, box, mitral isthmus line, bi-caval line, SCV	1 year: NSR without AAD
23	63	F	65	Parox	92	70/36	19,7	Yes	No	No	0	No	PVI, box, bicaval line	2 year: NSR without AAD
24	38	F	60	Parox	36	59/32	23,5	Yes	No	No	0	No	PVI, box, CTI	6 months: NSR without AAD
25	47	M	60	Parox	72	51/36	26,2	Yes	No	No	1	No	PVI, roof line	1 year: NSR without AAD
26	42	F	60	Parox	60	48/35	23,7	No	No	No	0	No	PVI, box, bicaval line, SCV	1 year: NSR without AAD

Baseline characteristics of all included patients with lesion set and follow-up results. No patient had previous cardiothoracic surgery or a cerebrovascular accident. Atrial fibrillation duration prior to intervention, is expressed in months.
BMI = body mass index, CA = catheter ablation, CAD = coronary artery disease, COPD = chronic obstructive pulmonary disease, EF = ejection fraction, F = female, M = male, NSR = normal sinus rhythm, Parox = paroxysmal, Pers = persistent, PVI = pulmonary vein isolation.

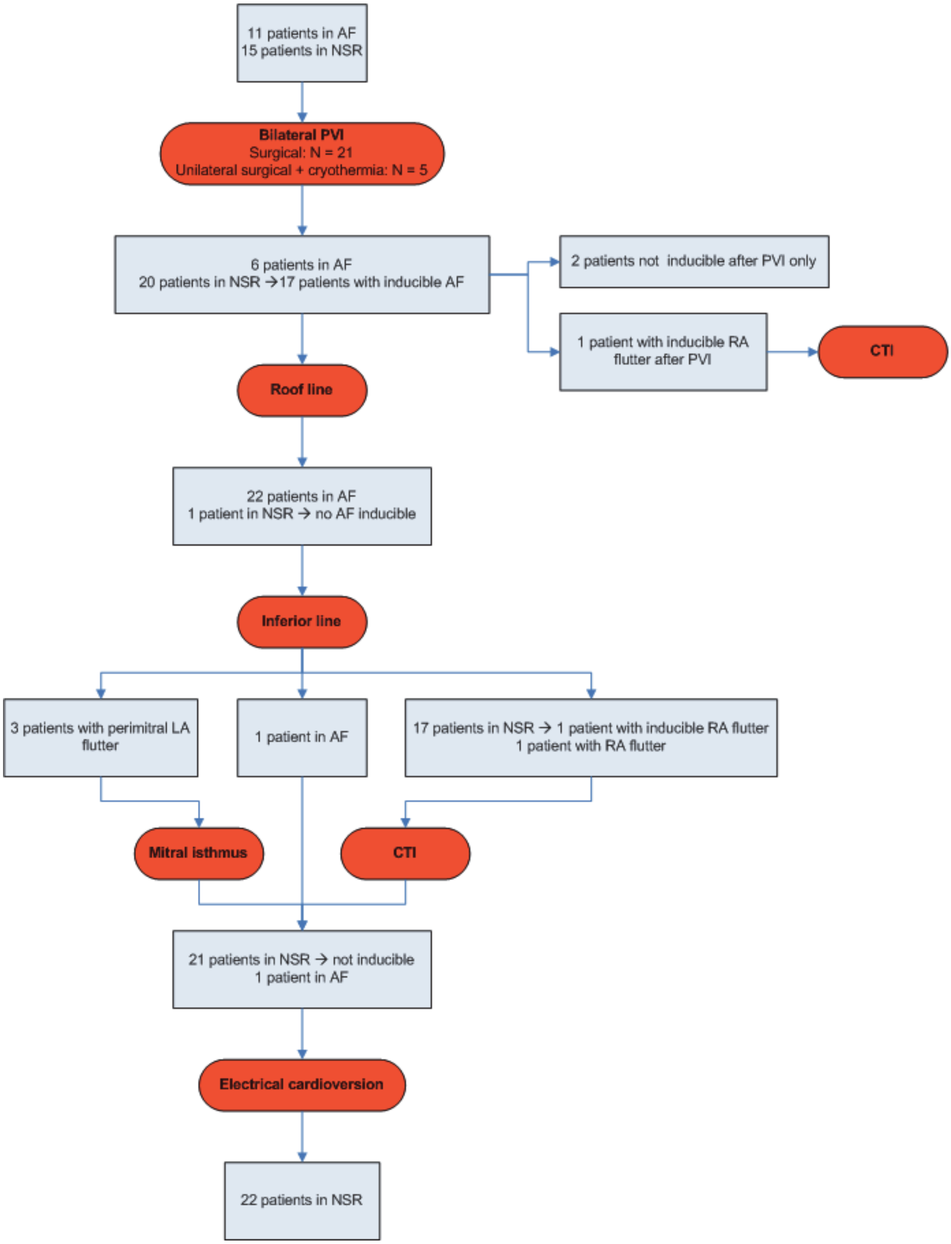


Figure 3. Flow Diagram of the Stepwise Lesion Sets See text for details. AF = atrial fibrillation, CTI = cavotricuspid isthmus, LA = left atrium, NSR = normal sinus rhythm, PVI = pulmonary vein isolation, RA = right atrium.

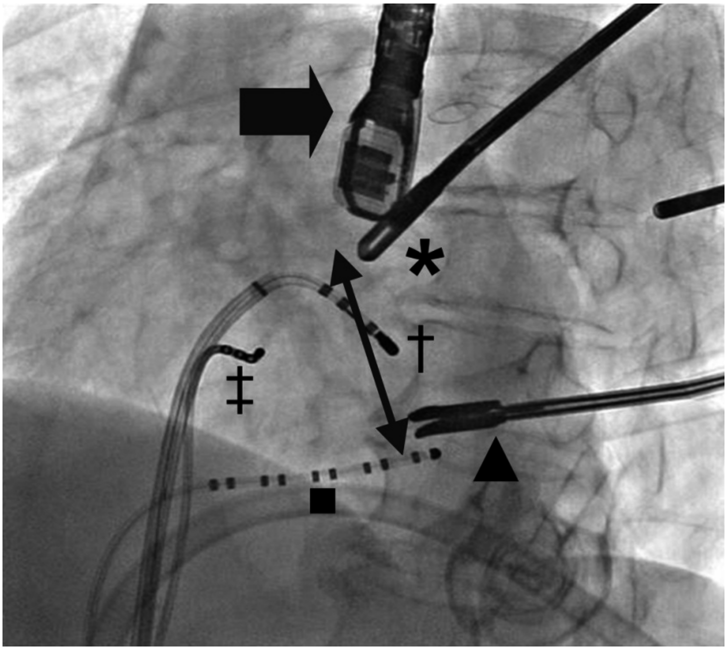


Figure 4. Linear Lesion at the Mitral Isthmus
Two instruments placed epicardially, visualise the location of this linear lesion (∗ = left inferior pulmonary vein, ▲ = coronary sinus). Bidirectional block across the mitral isthmus was determined using the following criteria: 1) widely separated double potentials along the whole linear lesion (↔), 2) pacing lateral to the line results in a proximal-to-distal activation sequence in the coronary sinus, 3) pacing immediately septal from this linear lesion with the coronary sinus catheter (■), results in late activation (170 to 190 ms) on the ablation catheter (†) at the lateral side of this line, 4) the conduction time from the septal side of the linear lesion to the lateral side gets shorter as the septal pacing site is moved further from the line. ‡ = His catheter, ➡ = transesophageal echocardiography probe.

Follow-up

Twenty-four (92%) patients reached 1 year follow-up and 96% underwent 7-days Holter monitoring 1 year after the procedure. The remaining 2 (8%) patients, reached 6 months follow-up and there was 100% compliance with 7-days Holter monitoring (Table 2).

At one year, 22 of 24 (92%) patients were in sinus rhythm with no episode of AF, AFL or AT lasting longer than 30 seconds on office follow-up, Holter monitoring or pacemaker interrogation (Figure 5). None of those patients was on AAD and 5 (21%) patients were on acenocoumarol. One-year success defined according to the Heart Rhythm Society/European Heart Rhythm Association/European Cardiac Arrhythmia Society consensus statement (freedom of AF/AFL/AT off AAD), was 93% for patients with paroxysmal AF and 90% for patients with persistent AF. Two (9%) of those 22 patients underwent CA for recurrent AF or left AFL after the hybrid procedure (Table 3). There was no statistically significant difference in patients with or without previous CA, regarding the presence of sinus rhythm after one year without AAD (p = 1.0).

Table 2. Monitoring

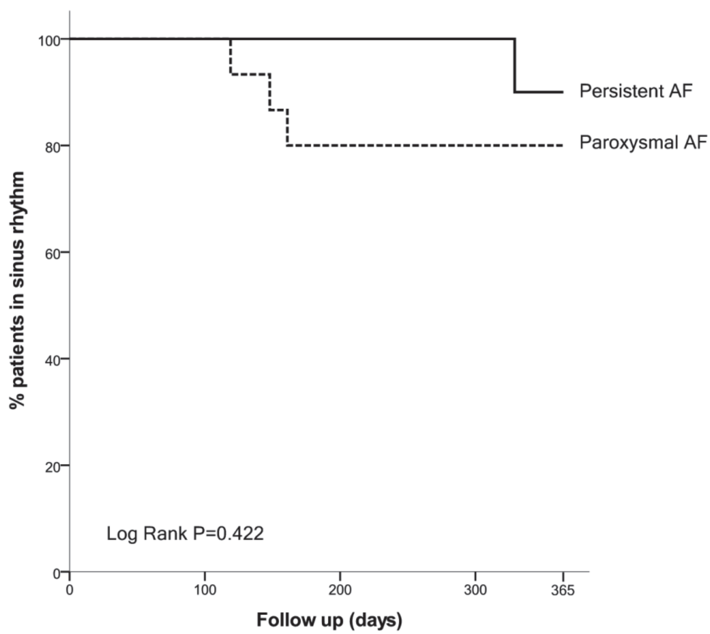
Patient	AF type	AAD before procedure	AAD stop (months)	Holter 3 months	Holter 6 months	Holter 9 months	Holter 12 months	Holter 24 months
1	Pers	sotalol	6	7 d , NSR	7 d, NSR	7 d, NSR	7 d, NSR	-
2	Pers	sotalol	6	48 h, NSR	7 d, NSR	NA	7 d, NSR	7 d, NSR
3	Pers	amiodarone	6	24 h, NSR	7 d, NSR	7 d, NSR	7 d, NSR	-
4	Pers	flecainide	not stopped	24 h, NSR	7 d, NSR	-	-	-
5	Pers	amiodarone	6	7 d, NSR	7 d, NSR	7 d, NSR	7 d, NSR	-
6	Pers	flecainide	6	48 h, NSR	7 d, NSR	7 d, NSR	7 d, NSR	-
7	Pers	propafenone	6	7 d, NSR	7 d, NSR	7 d, NSR	7 d, NSR	
8	Pers	disopyramide	6	7 d, NSR	7 d, NSR	NA	7 d, NSR	7 d, NSR
9	Pers	metoprolol	6	48 h, NSR	7 d, NSR	NA	7 d, NSR	-
10	Pers	amiodarone	6	7 d, NSR	7 d, NSR	7 d, NSR	7 d, NSR	-
11	Pers	amiodarone	6	7 d, NSR	7 d, NSR	7 d, NSR	7 d, NSR	-
12	Parox	flecainide	4	7 d, AFL	7 d, AFL	7 d, NSR	7 d, NSR	-
13	Parox	flecainide	6	48 h, NSR	48h, NSR	7 d, NSR	7 d, NSR	-
14	Parox	sotalol	6	48 h, NSR	7 d, NSR	7 d, NSR	7 d, NSR	-
15	Parox	sotalol	not stopped	7 d, PAF	7 d, NSR	7 d, NSR	7 d, PAF	-
16	Parox	amiodarone	6	7 d, NSR	7 d, NSR	7 d, NSR	7 d, NSR	-
17	Parox	amiodarone	6	7 d, NSR	NA	7 d, NSR	7 d, NSR	-
18	Parox	flecainide	3	PM, NSR	PM, NSR	PM, NSR	PM, NSR	-
19	Parox	flecainide	6	48 h, NSR	7 d, NSR	7 d, NSR	7 d, NSR	-
20	Parox	flecainide	6	7 d, NSR	7 d, NSR	7 d, NSR	7 d, NSR	-
21	Parox	metoprolol	6	7 d, NSR	7 d, NSR	NA	7 d, NSR	-
22	Parox	sotalol	6	7 d, NSR	7 d, NSR	7 d, NSR	7 d, NSR	-
23	Parox	flecainide	6	7 d, NSR	7 d, NSR	NA	7 d, NSR	7 d, NSR
24	Parox	disopyramide	6	7 d, NSR	7 d, NSR	-	-	-
25	Parox	sotalol	6	7 d, NSR	7 d, NSR	7 d, NSR	7 d, NSR	-
26	Parox	flecainide	3	7 d, NSR	7 d, NSR	NA	7 d, NSR	-

Anti-arrhythmic drug (AAD) use, type and result of monitoring in all included patients. The duration of AAD intake after the hybrid procedure (AAD stop) is given for each patient. Patient 6, 12, 15, and 17 had arrhythmia recurrence.
NA = not available, NSR = normal sinus rhythm, Parox = paroxysmal, Pers = persistent, PM = pacemaker, 24 h/48 h/7 d = 24 hours/48 hours/7 days continuous Holter monitoring.

Table 3. Supraventricular Tachycardia Recurrences after Hybrid Procedure and Management

Patient	Time to SVT Recurrence, days	Type of SVT	Mode of diagnosis	Management of recurrence	Recurrence after additional therapy	Follow-up after additional therapy	AAD after CA
6	329	AF	ECG	flecainide	PAF	4 months	
12	119	left atrial flutter	ECG	CA	none	5 months	none
15	148	AF	48 hours Holter	sotalol	rare and brief PAF	13 months	
17	161	AF	ECG	CA	none	8 months	none

PAF = paroxysmal atrial fibrillation.



Remaining cases paroxysmal AF	15	12	12	11
Remaining cases persistent AF	11	11	11	9

Figure 5. Outcome of Hybrid Ablation Procedure
Kaplan-Meier curve showing the outcomes of hybrid ablation procedure. At 1 year follow-up, hybrid ablation resulted in an overall single-procedure success rate of 83% (79% for paroxysmal atrial fibrillation (AF) and 90% for persistent AF). An event was considered a patient who, at any time, had recurrent supraventricular tachycardia.

This means a single-procedure success rate (sinus rhythm without AAD and/or redo procedure) of 79% at 1 year for paroxysmal AF (11 out of 14 patients) and 90% for persistent AF (9 out of 10 patients) and an overall single-procedure success rate of 83% at 1 year.

At six months, 2 of 2 (100%) patients were in sinus rhythm with no episode of AF, AFL or AT lasting longer than 30 seconds. One of those patients was taking flecainide and they both were on acenocoumarol. None of those patients had an additional CA procedure.

The management of patients with recurrent supraventricular tachycardia (SVT) after the three months blanking period, is summarized in Table 3. Four (15%) of 26 patients had SVT recurrence, with a mean of 99±94 (range, 29 to 239) SVT-free days after the blanking period. Two of these 4 patients underwent an electrophysiologic study and CA. One patient was found to have AF due to a gap at the junction of the right superior PV with the roof of the LA. The other patient had a left AFL. These 2 patients have been followed for at least five months and have not experienced any SVT anymore off AAD. The remaining 2 patients with SVT recurrence, are treated with AAD for paroxysmal AF.

Complications

No deaths or conversion to cardiopulmonary bypass were encountered. No patient demonstrated paralysis of the phrenic nerve. One patient had a pleural effusion drained 3 weeks after surgery. One patient stayed hospitalized for 13 days due to difficult to control chest pain at the insertion sites of the working ports without signs of infection.

Discussion

Main findings

This report describes for the first time the combined simultaneous thoracoscopic surgical and transvenous CA of paroxysmal and persistent AF. These two complementary techniques performed in combination, bear the potential of treating AF with one single ablation procedure. According to accepted definitions, our overall one-year freedom of arrhythmia without AADs was 92% with only 2 patients needing a second CA procedure (3). Of note, almost half persistent and over a third of patients had one or more previous CA. The robustness of the hybrid approach lies in its complimentary nature as represented by the fact that in almost a quarter of patients CA was needed to finish incomplete epicardial surgical lesions by endocardial touch-up, and additional lesions such as the mitral isthmus line can be performed rather fast.

Hybrid procedure versus percutaneous catheter ablation techniques

Jaïs et al found that if AF was inducible after PV isolation in patients with paroxysmal AF, the addition of linear lesions, with the endpoint of noninducibility, resulted in 91% of patients free from arrhythmia without AAD during a follow-up of 18±4 months (8). To reach that number, however, 31% of patients needed a second procedure. Using the same endpoint, our success percentage off AAD was comparable but only 9% of patients needed a second procedure.

The single-procedure, drug-free success rate of the stepwise ablation approach for persistent AF as described by Haïssaguerre et al, was 62% at 11± 6 months (9). Allowing for repeat procedures and the use of AAD, the one year success rate increased to 95%. In our series we followed a comparable ablation strategy and the single-procedure, drug-free success rate at one year was 83%. Allowing for redo-procedures, this number increased to 92%.

The hybrid approach appears to result in better endpoints regarding rhythm control, both for paroxysmal and persistent AF, using the same endpoints and ablation strategy as described in other trials.

Approximately 80% of patients have at least partial recovery of PV conduction at 4 months after PV isolation with unipolar RF (10). Bipolar RF energy, as used in our series, overcomes the heat-sink by clamping the tissue and excluding the effect of the circulating blood on ablation which seems to result in more persistent lesions (11). But even for such devices, epicardial fat can prevent transmurality. In our series, the box lesion was incomplete after epicardial ablation alone in 23% of the patients, i.e. endocardial touch-up with unipolar RF energy was necessary to achieve bidirectional block. The possibility to perform such an endocardial touch-up, is one of the major advantages of this procedure.

Hybrid procedure versus surgical ablation techniques

By replacing the incisions of the traditional Cox-maze III procedure with less invasive linear lesions of ablation using bipolar RF, Damiano et al introduced the Cox-maze IV procedure (12). This approach still requires cardiopulmonary bypass and at least one small right thoracotomy. The freedom of AF recurrence was 91% at 12 months and 67% of patients off AAD. These figures are comparable with our results although in the case of the hybrid procedure, no cardiopulmonary bypass is needed nor a thoracotomy. None of the existing surgical ablation technologies (even bipolar RF) can guarantee complete transmurality. We solved this issue by applying RF endocardially in the case of incomplete lesions. Another shortcoming of the surgical approach is the inability to precisely locate AF triggers and to map ATs or reentry arrhythmias known to occur during AF ablation (13). In the setting of a hybrid procedure however, it is possible to perform extensive mapping in order to tailor the lesion set. Finally, during an epicardial surgical AF ablation on the beating heart, it is technically not possible to create a linear lesion across the CTI. In our series, this was safely performed endocardially in 3 patients.

Hybrid procedure versus surgical ablation with epicardial mapping

In 2009, Lockwood et al described techniques for assessing conduction block across surgical lesions based on epicardial mapping (7). Using combinations of a focal and bipolar RF device as in our series, they achieved complete block across linear lesions by the first set of RF applications in only 21%. Several factors such as epicardial fat and local myocardial thickness, limit the depth of penetration of RF and thus the creation of transmural lesions (14). After localisation of the gaps, epicardial ablation was repeated until complete bidirectional block across all the linear lesions.

In our series, pacing manoeuvers and mapping techniques were performed from the endocardial side. In 23% of our patients we were not able to create a complete box lesion, even after repeating epicardial ablation. To create completely transmural lesions, we applied unipolar RF endocardially at the remaining gaps.

Krul et al described a series of 31 AF patients, treated with thoracoscopic PV isolation and ganglionated plexi ablation (15). In patients with nonparoxysmal AF, LA ablation lines were created and conduction block verified epicardially with custom made catheters. After 1 year, they reported comparable results to our series (86% of patients had no recurrence of SVT off AAD). Although the autonomic nervous system seems to play an important role in AF, there is up to now too little evidence to advocate a systematic ganglionated plexi ablation strategy (16,17). In animal models, return of ganglionated plexi activity was observed 4 weeks after selective ablation and little is known about the electrophysiological impact reinnervation will have on the long term outcome (18). An important conceptual difference between studies is that Krul et al. could only perform epicardial lesions without the possibility of add on endocardial lesions including endocardial touch-ups to improve transmurality, as well as performing CTI and left sided isthmus ablation. In addition, they could only check completeness of ablation lesions from the epicardium which may be insufficient to show complete electrical block.

Limitations

The low number of patients in this single-center retrospective study prevents definitive conclusions, also in view of the limited power of the log rank test we used to compare groups. However, future larger studies may corroborate our results.

Although patients with previous CA had at most a PV isolation procedure and none of the PVs appeared to be isolated in any of these patients, it cannot be excluded that previous CA favourably influenced the results.

The single procedure success rate was similar – rather than lower - in patients with persistent compared to those with paroxysmal AF. Although this may be due to low sample size, it may also be considered an expression of the robustness of the hybrid procedure.

In the current series, the overall clinical success may have not recognized some episodes of asymptomatic arrhythmia by the relatively short periods of ambulatory monitoring performed.

The safety of this procedure may be a concern because of the extent of ablation and the full heparinisation during the procedure.

The longer-term impact of this ablation strategy on the atrial systolic function remains unknown.

An ablation strategy based on non-inducibility, could lead to overtreatment of some patients. As demonstrated by Jaïs et al, despite being still inducible after PV isolation and deployment of linear lesions, some patients remained arrhythmia free without AAD (8).

Conclusions

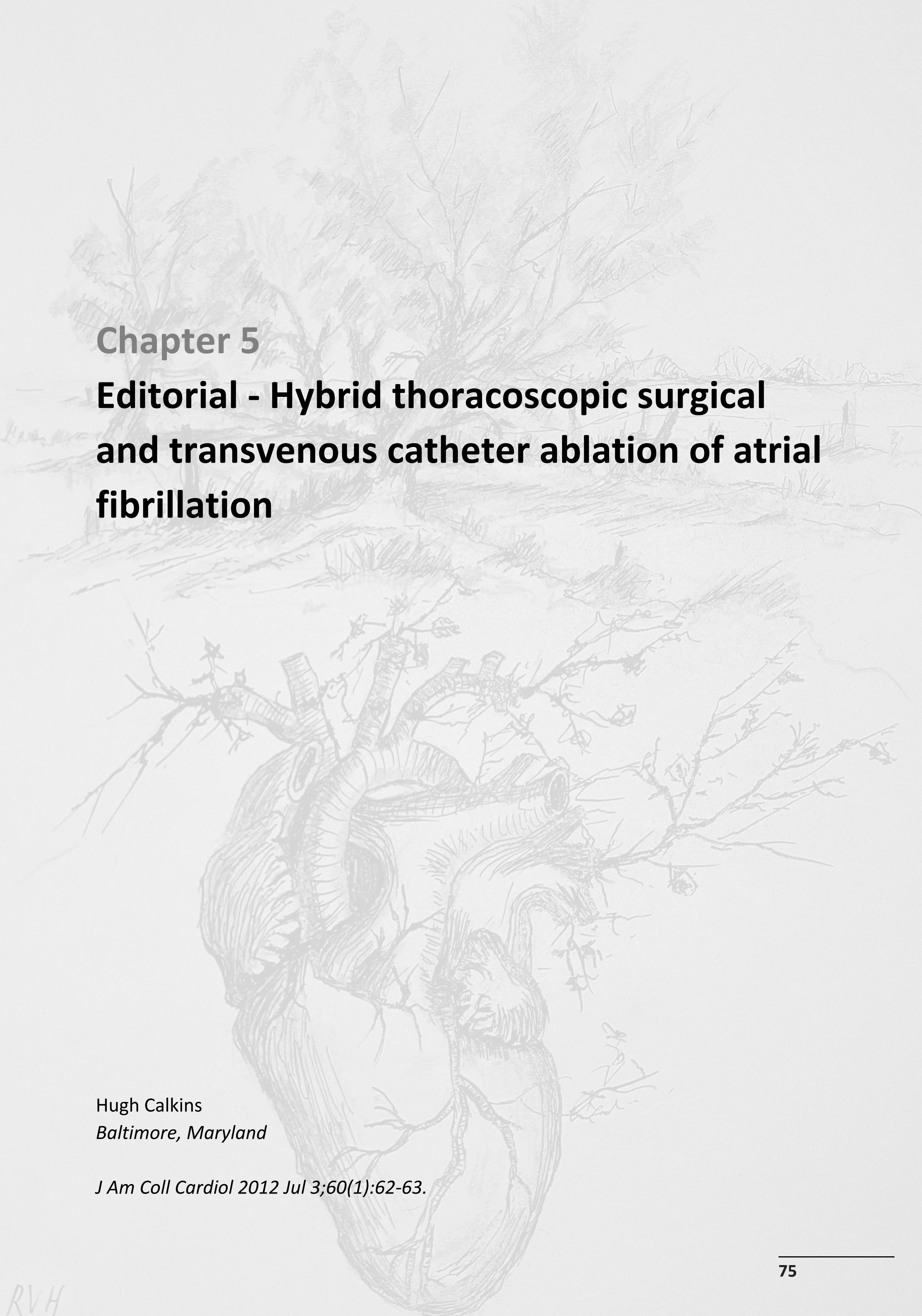
A combined transvenous endocardial and thoracoscopic epicardial ablation procedure for paroxysmal and recent persistent AF resistant to AAD, has a single-procedure success rate of 83% at one year. Recurrent arrhythmias can be handled with AAD or CA.

Abbrevations

AAD = anti-arrhythmic drug
AF = atrial fibrillation
AFL = atrial flutter
AT = atrial tachycardia
CA = catheter ablation
CTI = cavotricuspid isthmus
LA = left atrium
PV = pulmonary vein
RF = radiofrequency
SVT = supraventricular tachycardia

References

1. Nault I, Miyazaki S, Forclaz A, et al. Drugs vs. ablation for the treatment of atrial fibrillation: the evidence supporting catheter ablation. Eur Heart J 2010;31:1046-1054.
2. Callans DJ, Gerstenfeld EP, Dixit S, et al. Efficacy of repeat pulmonary vein isolation procedures in patients with recurrent atrial fibrillation. J Cardiovasc Electrophysiol 2004;15:1050-1055.
3. Calkins H, Brugada J, Packer DL, et al. HRS/EHRA/ECAS expert consensus statement on catheter and surgical ablation of atrial fibrillation: recommendations for personnel, policy, procedures, and follow-up: a report of the Heart Rhythm Society Task Force on Catheter and Surgical Ablation of Atrial Fibrillation. Heart Rhythm 2007;4:816–861.
4. Oral H, Knight BP, Tada H, et al. Pulmonary vein isolation for paroxysmal and persistent atrial fibrillation. Circulation 2002;105:1077-1081.
5. Wolf RK, Schneeberger EW, Osterday R, et al. Video-assisted bilateral pulmonary vein isolation and left atrial appendage exclusion for atrial fibrillation. J Thorac Cardiovasc Surg 2005;130:797-802.
6. Bugge E, Nicholson IA, Thomas SP. Comparison of bipolar and unipolar radiofrequency ablation in an in vivo experimental model. Eur J Cardiothorac Surg 2005;28:76-82.
7. Lockwood D, Nakagawa H, Peyton MD, et al. Linear left atrial lesions in minimally invasive surgical ablation of persistent atrial fibrillation: Techniques for assessing conduction block across surgical lesions. Heart Rhythm 2009;6:S50-63.
8. Jaïs P, Hocini M, Sanders P, et al. Long-term evaluation of atrial fibrillation ablation guided by noninducibility. Heart Rhythm 2006;3:140-145.
9. Haïssaguerre M, Hocini M, Sanders P, et al. Catheter ablation of long-lasting persistent atrial fibrillation : clinical outcome and mechanisms of subsequent arrythmias. J Cardiovasc Electrophysiol 2005;16:1138-1147.
10. Cappato R, Negroni S, Pecora D, et al. Prospective assessment of late conduction recurrence across radiofrequency lesions producing electrical disconnection at the pulmonary vein ostium in patients with atrial fibrillation. Circulation 2003;108:1599-1604.
11. Melby SJ, Gaynor SL, Lubahn JG, et al. Efficacy and safety of right and left atrial ablations on the beating heart with irrigated bipolar radiofrequency energy: a long-term animal study. J Thorac Cardiovasc Surg 2006;132:853-860.
12. Shen J, Bailey MS, Damiano RJ. The surgical treatment of atrial fibrillation. Heart Rhythm 2009;6:S45-50.
13. Jaïs P, Matsuo S, Knecht S, et al. A deductive mapping strategy for atrial tachycardia following atrial fibrillation ablation: Importance of localized reentry. J Cardiovasc Electrophysiol 2009:20;480-491.
14. Thomas SP, Guy DJ, Boyd AC, Eipper VE, Ross DL, Chard RB. Comparison of epicardial and endocardial linear ablation using handheld probes. Ann Thorac Surg 2003;75:543-548.
15. Krul SP, Driessen AH, van Boven WJ, et al. Thoracoscopic video-assisted pulmonary vein antrum isolation, ganglionated plexus ablation, and periprocedural confirmation of ablation lesions. Circ Arrhythm Electrophysiol 2011;4:262-270.
16. Schauerte P, Scherlag BJ, Patterson E, et al. Focal atrial fibrillation: experimentel evidence for pathophysiologic role of the autonomic nervous system. J Cardiovasc Electrophysiol 2001;12:592-599.
17. De Ferrari GM, Schwartz PJ. Autonomic nervous system and arrhythmias. Ann N Y Acad Sci 1990;601:247-262.
18. Sakamoto S, Schuessler RB, Lee AM, Aziz A, Lall SC, Damiano RJ. Vagal denervation and reinnervation after ablation of ganglionated plexi. J Thorac Cardiovasc Surg 2010;139:444-452.



Chapter 5

Editorial - Hybrid thoracoscopic surgical and transvenous catheter ablation of atrial fibrillation

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During the past decade, catheter ablation of atrial fibrillation (AF) has emerged as an important treatment option for patients with symptomatic AF refractory to 1 or more antiarrhythmic agents. Electrical isolation of the pulmonary vein musculature (PVI) has been identified as the primary end point for both catheter-based and surgical AF ablation procedures (1). Despite the widespread adoption of catheter ablation for treatment of patients with AF, the long-term efficacy of the procedure needs to improve, especially for patients with persistent and long-standing persistent AF.

In this issue of the *Journal*, Pison et al. (2) report the results of an ambitious prospective single-center study of 26 consecutive patients who underwent a hybrid thoracoscopic surgical and transvenous catheter ablation procedure over a 21-month period. These patients were followed closely for a mean of 470 ± 154 days with serial 7-day Holter monitoring. Ablation success was defined in accordance with the Heart Rhythm Society, European Heart Rhythm Association, and European Cardiac Arrhythmia Society consensus document as freedom from AF, atrial flutter, or atrial tachycardia lasting 30 seconds or longer after a 3-month blanking period. Fifteen patients had paroxysmal AF, 10 persistent AF, and 1 long-standing persistent AF. One or more catheter ablation procedures had previously failed in 10 patients. The ablation strategy involved a combined minimally invasive, off-pump thoracoscopic surgical approach using the Atricure bipolar radiofrequency clamp (Atricure, West Chester, Ohio), a bipolar radiofrequency linear pen, and a conventional endocardial irrigated radiofrequency catheter ablation system (ThermoCool, Biosense Webster, Diamond Bar, California). The use of endocardial catheter ablation allowed the completion of lesion sets that could not be completed surgically, especially the mitral isthmus line and the cavotricuspid isthmus ablation line. Endocardial ablation, guided by epicardial mapping rather than a 3-dimensional mapping system, was also used to fill gaps in the surgically applied lesions. The precise lesion set in a given patient was tailored on the basis of concomitant disease (patients with chronic obstructive pulmonary disease had the left pulmonary veins isolated with a cryoballoon, PVI in 26, posterior box in 22, bicaval line in 9, mitral isthmus in 3, and CTI in 3). The mean procedure time was 280 ± 84 min, with a range of 195 to 505 min. Follow-up visits, which included 7-day Holter monitoring, were set up at 3, 6, 9, 12, and 18 months after ablation. All procedures were performed at a single center by the same cardiac surgeon and electrophysiologist.

The single procedure success rate was 83%. With the inclusion of repeat endocardial ablation procedures performed in 2 patients, the success rate increased to 92%.

The only complication that occurred was a pleural effusion requiring drainage in 1 patient. The investigators conclude that a combined transvenous endocardial and thoracoscopic epicardial ablation procedure for paroxysmal and recent persistent AF has a single-procedure success rate of 83% at 1 year and that recurrent arrhythmias can be addressed with catheter ablation or antiarrhythmic drug therapy. This landmark study is a welcome addition to the published research on catheter and surgical AF ablation. I commend Pison et al. (2) for their enormous efforts to complete this novel clinical trial.

Despite the small number of patients, the duration, intensity of monitoring, and completeness of follow-up are to be commended. The remarkably low complication rate speaks to the expertise of the operators and center and is also to be congratulated. In writing this editorial, I am charged with helping interpret the results of this study in the context of both my own experience with catheter ablation as well as the considerable body of previously published research on catheter and surgical AF ablation. I would like to offer 2 thoughts for readers' consideration.

It must be recognized and appreciated that this is the first publication to report the outcomes of a "hybrid" thoracoscopic surgical and transvenous catheter ablation procedure for AF. As outlined in the report, there exists a clear rationale for this approach, as some ablation lesions that are incorporated into the well-established Cox maze lesion cannot be accomplished using a minimally invasive, offpump surgical approach. And other lesions that are part of this ablation strategy may be more successfully applied using currently available surgical ablation tools (i.e., PVI, where the rate of permanent long-term PVI with catheter ablation is limited). Consistent with their hypothesis was the very high single-procedure efficacy of this approach. However, the enthusiasm for this "hybrid" ablation strategy must be tempered by some important limitations that must be recognized with both the ablation strategy and the design of this study. It is unfortunate that the investigators did not choose to take on a series of patients with long-standing persistent AF, especially a series of patients with longstanding AF of many years' duration and dilated left atria, for it is in this subset of patients that the results of catheter ablation have been most disappointing. Hopefully, the investigators are carrying out this trial at the present time. Another limitation of the "hybrid" ablation strategy is that it is a logistical nightmare. Not only are experts in both catheter ablation and surgical ablation required, but they must both be available in the same hospital, on the same day, at the same time, and for as long as 8 h (the longest procedure in this report required 505 min). This may explain why it required 21 months to perform the 26 procedures in this trial. It is my impression that it is extremely rare to have tremendous expertise with catheter ablation and surgical AF ablation at the same institution.

Most centers are expert at one or the other. Further studies need to examine the feasibility of a staged hybrid approach, in which the surgical ablation is performed on a separate day from the catheter ablation part of the study. Once a staged strategy is considered, one wonders if it would be preferable to perform the surgical ablation with PVI first and perform the catheter ablation part of the procedure only if AF recurs after the initial surgical procedure. I suspect that for some patients, all that is needed is PVI. The remarkably high ablation success rate reported in this trial is truly remarkable. This important result has implications for the entire field of AF ablation, because it is further evidence that AF ablation procedures that are based on the cornerstone of PVI are effective, especially for treatment of patients with paroxysmal and early persistent AF.

And when performed by highly experienced operators at experienced centers, these procedures can be performed safely.

What remains less clear is the important issue of which lesions or lesion sets are needed and what is the best end point for the procedure. This study does little to provide new knowledge that can be applied to this important question. This statement reflects the fact that most patients in this series had paroxysmal AF, and only 1 patient had long-standing persistent AF. Furthermore, ablation lesions with the exception of PVI were "tailored" on the basis of inducibility, concomitant patient diseases, AF type, and operator preference. The resultant "special sauce" applied to each patient may not be replicable by other centers and operators. As noted previously and shown on a patient-bypatient basis in Table 1 of the report (2), the only standard lesion applied to all patients was PVI. Despite the theoretical benefit of a hybrid approach to accomplish a complete mitral line and cavotricuspid line, these lesions were each created in only 3 of the 26 patients.

At the end of the day, is hybrid thoracoscopic and transvenous catheter ablation of AF the answer we are searching for? In my opinion, the answer is "not yet," and certainly not on the basis of the very limited worldwide experience with this approach. It is clear that more research is needed. In particular, I would like to see the results of a much larger, multicenter trial of "hybrid AF ablation" that targets a population of patients with long-standing persistent AF and dilated left atria. Those involved in this field are grateful to Pison et al. (2) for bringing forth the concept of "hybrid AF ablation."

References

1. Calkins H, Kuck KH, Cappato R, et al. 2012 HRS/EHRA/ECAS expert consensus statement on catheter and surgical ablation of atrial fibrillation: recommendations for patient selection, procedural techniques, patient management and follow-up, definitions, endpoints, and research trial design: a report of the Heart Rhythm Society (HRS) Task Force on Catheter and Surgical Ablation of Atrial Fibrillation. Developed in partnership with the European Heart Rhythm Association (EHRA), a registered branch of the European Society of Cardiology (ESC) and the European Cardiac Arrhythmia Society (ECAS); and in collaboration with the American College of Cardiology (ACC), American Heart Association (AHA), the Asia Pacific Heart Rhythm Society (APHRS), and the Society of Thoracic Surgeons (STS). Endorsed by the governing bodies of the American College of Cardiology Foundation, the American Heart Association, the European Cardiac Arrhythmia Society, the European Heart Rhythm Association, the Society of Thoracic Surgeons, the Asia Pacific Heart Rhythm Society, and the Heart Rhythm Society. Heart Rhythm 2012;9:632–96.
2. Pison L, La Meir M, van Opstal J, Blaauw Y, Maessen J, Crijns HJ. Hybrid thoracoscopic surgical and transvenous catheter ablation of atrial fibrillation. J Am Coll Cardiol 2012;60:54–61.

Chapter 6

Safety and feasibility of adenosine administration during hybrid atrial fibrillation ablation to test dormant pulmonary vein conduction

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Submitted

Abstract

Background

Adenosine administration after initial pulmonary vein (PV) isolation reveals dormant conduction and predicts atrial fibrillation (AF) recurrence. This testing may increase long term success rate of AF ablation procedures. There are no studies till date using adenosine to reveal acute reconduction of PVs after epicardial PV isolation during hybrid AF ablation procedure.

Methods and Results

We included 20 patients (17 male, 56±9 years) undergoing hybrid ablation for symptomatic paroxysmal (n =10) and persistent (n=10) AF, using an epicardial bipolar radiofrequency clamp to perform PV isolation. All anti-arrhythmic medications were stopped 5 days prior to the procedure except for patients on amiodarone. Thirty minutes after PV isolation, and once sinus rhythm was obtained with other linear ablation lesions and electrical cardioversion if necessary, a bolus of adenosine (12 to 36 mg) was administered intravenously. The subsequent response was assessed for each PV (n=84) using an in-situ circular mapping catheter. If reconduction was seen, further endocardial ablation using a 3.5 mm irrigated tip catheter was performed until no more reconduction occurred after repeat adenosine bolus.

Conclusions

Adenosine administration after PV isolation with the use of an epicardial bipolar radiofrequency clamp in the setting of hybrid AF ablation, is feasible and safe and reveals acute reconduction in 1% of the PVs.

The cornerstone of endocardial catheter ablation procedures for atrial fibrillation (AF) is ablation of the ostium or antrum of the pulmonary veins (PV) with the endpoint of electrical isolation of these veins from the left atrium (LA). The rationale for this, is the seminal observation by Haissaguerre et al. in 1998 that AF was almost always triggered by ectopic beats arising from the muscle sleeves of the PVs.[1] The success rate of PV isolation in patients with paroxysmal AF, is greater than 80% and the most frequent reason for AF recurrence is PV reconduction.[2, 3] Adenosine is regularly used following initial PV isolation to unmask dormant PV conduction.[4] Additional ablation at sites with acute reconnection, may improve single procedure success rates.[5, 6]

Although being common practice during endocardial catheter ablation procedures, there is no data about the safety and feasibility of adenosine administration as a strategy to asses for transient PV reconnection during hybrid thoracoscopic surgical and transvenous catheter ablation procedures for atrial fibrillation.

Methods

Patient characteristics

Twenty consecutive patients with symptomatic AF underwent hybrid thoracoscopic surgical and transvenous catheter ablation. Selection criteria for this procedure were previously failed catheter ablation, failure of at least one antiarrhythmic drug (AAD), LA volume ≥ 29 ml/m2, persistent or longstanding persistent AF, or patient preference for a hybrid procedure instead of a percutaneous approach. Fourteen patients (70%) had prior catheter ablation for AF or atrial flutter (AFL). All patients underwent transthoracic echocardiography, cardiac computed tomography, and pulmonary function testing preoperatively. Definitions of paroxysmal, persistent, and longstanding persistent AF, success and failure of ablation, and follow-up monitoring were based on the Heart Rhythm Society, European Heart Rhythm Association, and European Cardiac Arrhythmia Society consensus statement.[7]

Hybrid ablation procedure

The hybrid ablation procedure was undertaken in a manner as described in detail elsewhere.[8] Briefly, 1 working port and 2 camera ports were inserted on both sides of the thorax in order to open the pericardium and the transverse and oblique sinuses during selective lung ventilation. Via the femoral venous approach, a His bundle (St. Jude Medical, St. Paul, Minnesota) and coronary sinus catheter (Medtronic, Minneapolis, Minnesota) were placed under fluoroscopy, and transseptal puncture was performed with a long 8-F sheath (SL0, St. Jude Medical) into the LA, followed by full heparinization. The PVs were mapped with a circular mapping catheter (Lasso, Biosense Webster, Diamond

Bar, California). Antral isolation of the right and left PVs as a pair was performed with a bipolar radiofrequency (RF) clamp (Atricure, West Chester, Ohio). Each application had a duration of about 15 seconds, with a median output of 10 to 15 W. The end point for PV ablation was entrance and exit block. In the case of sinus rhythm after PV isolation, reinduction of AF was attempted 5 times by pacing in the coronary sinus for 10 seconds at the shortest cycle length resulting in 1:1 atrial capture. AF was considered inducible if it lasted more than 1 min. If AF became noninducible, isoproterenol was infused at rates of 10 to 30 µg/min. If AF had not terminated or still was inducible, linear lesions were deployed. A roof line (connecting both superior PVs) and an inferior line (connecting both inferior PVs) were made epicardially using a bipolar RF pen or linear pen device (Isolater Pen and Coolrail; Atricure). These two linear lesions, in combination with bilateral antral PV isolation, result in complete electrical isolation of the posterior LA (box lesion). Any conduction gap in these epicardial linear lesions was ablated endocardially with a 3.5-mm-tip catheter (Thermo-Cool; Biosense Webster). If the patient was known to have typical AFL or if this arrhythmia occurred during the procedure, the cavotricuspid isthmus (CTI) was ablated endocardially. If the right atrium was dilated, 2 additional epicardial ablation lines were placed: one encircling the superior caval vein and the other connecting both caval veins. Patients still in AF after PVI and deployment of linear lesions, underwent electrical cardioversion. The left atrial appendage was excluded using a clipping device (Atriclip; Atricure) in 12 patients. The pericardium was approximated with a stitch, and a chest tube was placed in both pleural cavities.

Adenosine administration

All PVs were assessed selectively and sequentially in each patient with a circular mapping catheter at least 30 minutes after epicardial PV isolation and restoration of sinus rhythm. For each PV, a bolus of adenosine (12mg at least) was given intravenously. If necessary, this bolus was repeated with a higher dose until at least one blocked P wave occurred or a pause ≥ 3 seconds. Dormant conduction was defined as the reappearance of PV potentials during at least one beat. In the event of dormant conduction, selective endocardial ablation at sites of reconduction was performed. After additional endocardial ablation, adenosine administration was repeated.

Postablation care and follow-up

Low–molecular weight heparin was started 6 h after the procedure, and on the second post-operative day, acenocoumarol was reinitiated. Patients restarted as soon as possible their pre-operative AAD regimens. Any symptomatic patient not in sinus rhythm was cardioverted before the 3-month follow-up visit. One patient had a pacemaker, which was used for monitoring. The remaining patients underwent 7-day continuous Holter monitoring at 3, 6, 9, and 12 months. If 7-day Holter monitoring was not available, patients underwent at least 24 or 48-h Holter monitoring. According to current guidelines, success was defined as no episode of AF, AFL, or any atrial tachycardia (AT) lasting more than 30 seconds off AAD after the 3-month blanking period. Acenocoumarol and AADs were discontinued after the 6-month monitoring visit confirmed the absence of atrial arrhythmia.

Statistical analysis

Data were prospectively entered into a database. Statistical analysis was performed using SPSS version 20.0 (SPSS, Inc., Chicago, Illinois). Continuous variables are summarized with means and standard deviations. Any episode of AF, AFL, or AT lasting more than 30 seconds detected after the 3-month postprocedural period by electrocardiography, pacemaker interrogation, or 7-day, 48-h, or 24-h continuous Holter monitoring performed at 3, 6, 9, and 12 months was considered failure.

Results

Perioperative results

Twenty patients underwent hybrid procedures between September 17, 2012, and August 12, 2013. All AADs were stopped 5 days prior to the procedure except for patients on amiodarone. Patients' baseline characteristics are shown in Table 1. Nine patients had persistent AF, and 1 had longstanding persistent AF. Fourteen patients had 1 or more previous catheter ablation procedures. None of the PVs were isolated in those patients. Eight patients were in AF at the start of the procedure. In all patients, we achieved bidirectional block of all the PVs. For the left sided PVs, a mean of 7±2 RF applications were performed with a mean duration of 10±4 seconds. For the rightsided PVs, a mean 7±1 RF applications were performed with a mean duration of 9±4 seconds. In one patient, we did not deploy any other lesion because no arrhythmia was inducible. A box lesion was created epicardially in 19 patients. In 11 patients (58%), we were able to demonstrate endocardial entrance and exit block in the box during sinus rhythm. After endocardial touch-up in 8 patients (42%), we completed the box lesion. Five patients needed an endocardial touch-up at the roof line and 3 at both the roof and inferior line. In 7 patients, we created a bicaval line epicardially and isolated the superior caval vein. The cavotricuspid isthmus was ablated endocardially in 4 patients. Three patients (patient #2, #5 and #15) needed electrical cardioversion at the end of the procedure to restore sinus rhythm. All the other patients were in sinus rhythm.

Table 1. Baseline characteristics

Patient #	Age (yrs)	Gender	EF (%)	AF type	AF duration (months)	LA volume (ml)/ lpsa (mm)	AAD before procedure	BMI (kg/m^2)	Previous CA	Hyper-tension	CAD	Lesion set	Follow-up
1	53	M	37	Parox	24	75/38	amiodarone	32.1	Yes	No	Yes	PVI, box	1 yr: NSR without AAD
2	61	F	52	Pers	240	100/42	flecainide	39.1	Yes	Yes	No	PVI, box	1 yr: NSR with AAD
3	65	M	58	Pers	132	100/40	none	26	No	No	Yes	PVI, box, bicaval line, SCV, CTI	1 yr: NSR without AAD
4	41	M	50	Parox	131	126/48	flecainide	28.5	Yes	No	No	PVI, box	9 m: AF with AAD
5	54	M	46	Pers	156	99/57	sotalol	28	Yes	No	Yes	PVI, box, bicaval line, SCV, CTI	9 m: NSR without AAD
6	43	M	55	Parox	24	101/51	none	25.7	No	No	No	PVI, box, bicaval line, SCV	9 m: NSR without AAD
7	49	M	54	Parox	60	83/51	flecainide, sotalol	24.4	Yes	No	No	PVI, box, bicaval line, SCV	9 m: NSR with AAD
8	52	M	50	Parox	36	94/52	flecainide	29	Yes	No	Yes	PVI, box	9 m: NSR without AAD
9	63	M	68	Parox	84	105/52	flecainide	24.7	Yes	No	Yes	PVI, box	9 m: NSR without AAD
10	61	M	42	Pers	108	131/51	amiodarone	26.6	No	No	No	PVI, box, CTI	9 m: NSR without AAD
11	67	M	63	Parox	108	68/45	amiodarone	30.3	No	Yes	Yes	PVI, box	9 m: NSR with AAD
12	62	M	47	LS Pers	48	75/46	none	28.3	No	Yes	Yes	PVI, box	9 m: NSR with AAD
13	55	M	70	Parox	180	77/38	sotalol	28.7	Yes	Yes	Yes	PVI, box	6 m: NSR without AAD
14	60	F	50	Pers	60	104/39	sotalol	26.2	No	Yes	Yes	PVI, box	6 m: NSR without AAD
15	72	F	57	Pers	120	67/41	flecainide	27	Yes	Yes	No	PVI, box, bicaval line, SCV	6 m: NSR without AAD
16	56	M	60	Parox	24	112/38	none	21.6	Yes	No	No	PVI, box, bicaval line, SCV, CTI	3 m: NSR without AAD
17	55	M	46	Pers	24	84/51	none	32.3	Yes	Yes	Yes	PVI, box, bicaval line, SCV	-
18	49	M	56	Pers	48	53/35	none	31.7	Yes	No	No	PVI, box	-
19	65	M	65	Parox	72	66/44	sotalol	25.4	Yes	No	No	PVI	-
20	38	M	59	Pers	36	78/47	flecainide	26.3	yes	No	yes	PVI, box	-

Baseline characteristics of all included patients with lesion set and follow-up results.

AAD = antiarrhythmic drug; AF = atrial fibrillation; BMI = body mass index; CA = catheter ablation; CAD = coronary artery disease; CTI = cavotricuspid isthmus; EF = ejection fraction; LA = left atrial; lpsa = left parasternal axis; m = months; NSR = normal sinus rhythm; Parox = paroxysmal; Pers = persistent; LS Pers = longstanding persistent; PVI = pulmonary vein isolation; SCV = superior caval vein; yrs = years

Acute reconnection after adenosine administration

At least thirty minutes after PV isolation, and once sinus rhythm was obtained with other ablation lesions and electrical cardioversion if necessary, a lasso catheter was placed sequentially at the ostium of each PV. All the pulmonary veins (n=84) still displayed entrance and exit block at that point in time. For each PV, an adenosine bolus of at least 12 mg was injected through the right jugular vein, followed by a saline flush in order to block at least one P wave or to induce a pause ≥ 3 seconds. If necessary, this bolus was repeated with a higher dose (Table 2). Dormant conduction induced by adenosine administration (i.e., the reappearance of PV potentials during at least one beat) was seen in 1 out of 84 PVs (1%)(Figure 1). It occurred in patient #14 at the junction of the left superior PV ostium with the roof of the LA. Additional endocardial ablations were performed at this site (Figure 2). Repeating the administration of adenosine, did not result anymore in acute reconnection.

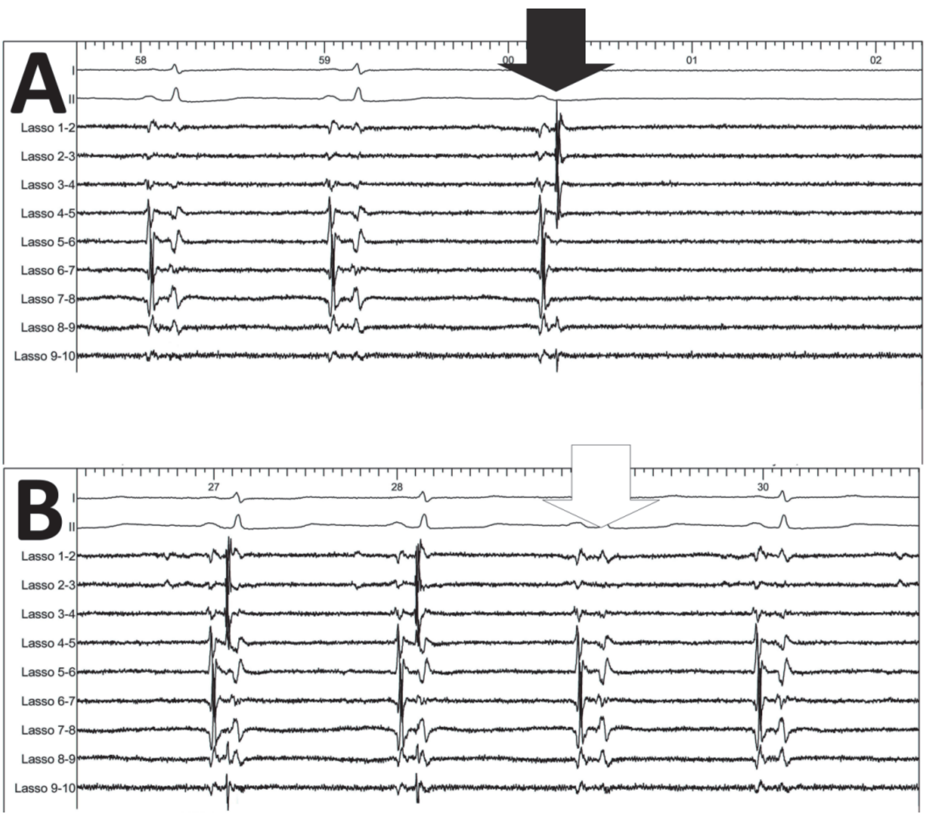


Figure 1. The administration of 21 mg of adenosine in patient #14 induced transient AV block and the transient reappearance of PV potentials (black arrow) on the circular mapping catheter (Lasso) at the first blocked P-wave. Twelve seconds later the PV potentials disappeared (white arrow).

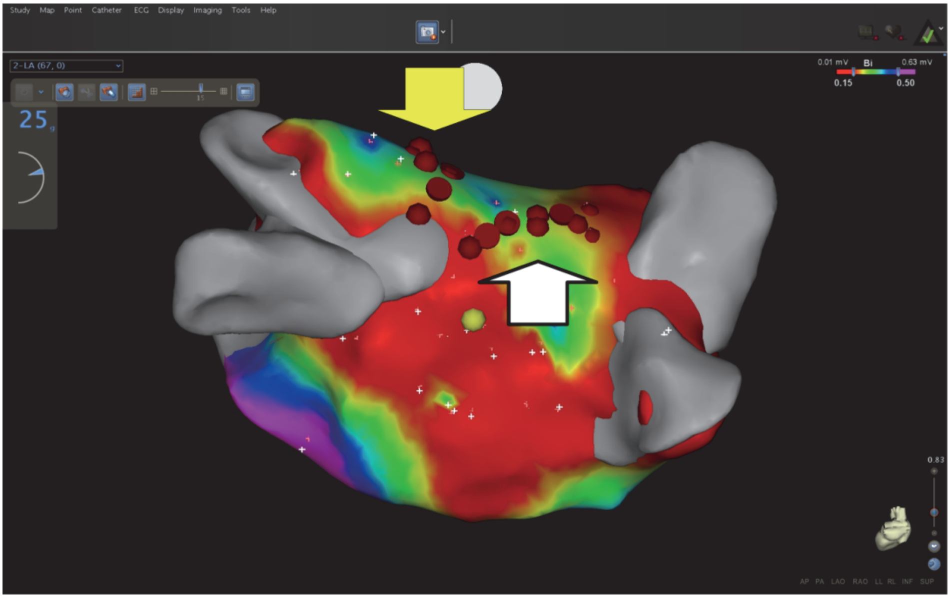


Figure 2. Posterior view of the LA voltage map in patient #14. The RF applications at the junction of the left super superior PV with the roof of the LA are visualized (yellow arrow). In this patient, endocardial RF touch-up of the roofline was necessary to complete the box lesion (white arrow).

Table 2. Adenosine dose per pulmonary vein

Left superior PV	17±5mg (range 12-30)
Left inferior PV	17±6mg (range 12-36)
Right superior PV	15±3mg (range 12-21)
Right inferior PV	15±3mg (range 12-21)

Mean adenosine dose per pulmonary vein (PV)

Long-term follow-up

Three patients (15%) reached 1-year follow-up, 9 (45%) reached 9-months and the remaining 8 (40%) reached 6-months or less. At 1 year, all 3 patients (100%) were in sinus rhythm, with no episodes of AF, AFL, or AT lasting longer than 30 seconds on office follow-up and Holter monitoring (Table 1). One of these patients was still on AADs.

Complications

No deaths or conversion to cardiopulmonary bypass were encountered. No patient demonstrated paralysis of the phrenic nerve. The administration of adenosine, did not result in any significant hemodynamic instability nor arrhythmia.

Discussion

The major findings of this study were as follows:

1. The use of adenosine during hybrid ablation for AF as a tool to check for dormant PV conduction after epicardial PV isolation, is feasible and safe.
2. Adenosine reveals dormant conduction in only 1% of the PVs after epicardial PV isolation, indicating extremely efficient PV isolation using epicardial bipolar and bilateral RF ablation.

Pulmonary vein reconnection after initial PV isolation, remains the most important reason for AF recurrence.[7] It is present in more than 80% of patients who undergo a repeat procedure.[9-11] This phenomenon still remains one of the 'Achilles heels' of modern invasive electrophysiology. New energy sources and balloon-based devices have been developed to improve long-term results of PV isolation, but it is too early to draw definitive conclusions.[12, 13] Contact catheter technology is also promising and may provide more longlasting lesions but there is no long-term data available yet.[14]

Dormant conduction is the phenomenon of transiently restored conduction through a previously isolated PV, induced by an intravenous purinergic agonists such as adenosine. The use of adenosine as a provocative measure to unmask the presence of dormant conduction after PV isolation, was first studied by Arentz et al. in 2004.[5] They showed that after successful ostial PV isolation, 25% of the studied PVs regained electrical activity after the administration of adenosine. Since this observation, the use of this drug during PV isolation procedures, became common clinical practice. Datino et al. described the mechanisms by which adenosine restores dormant PV conduction by recording action potentials from canine LA and PV cells.[15] The restoration of conduction in damaged but viable PVs, is based on selective activation of the I_{KAdo} inward rectifier current, resulting in hyperpolarization of the resting membrane potential. As PVs with dormant conduction are characterised by less resting membrane depolarization than veins without dormant conduction, the adenosine-induced hyperpolarization will selectively restore excitability in dormant conduction PVs by removing voltage-dependent I_{Na} inactivation.

McLellan et al. published very recently a systematic review on the use of adenosine after PV isolation.[4] Several interesting observations from this paper are worth highlighting. Data from nonrandomized and retrospective studies, showed that patients undergoing adenosine testing and ablation of reconnections had better outcomes than patients in whom adenosine testing was not used. However, in patients with acute reconnection after adenosine and additional ablation at these sites, the occurrence of recurrent AF tended to be higher than in patients without acute reconnection. The reason for this finding remains unclear. A possible explanation could be that acute reconnection is a surrogate marker of the impossibility to create completely transmural circular lesions, e.g. because of anatomic reasons.[16] The ADVICE trial is a prospective and randomized study, designed to analyse the effects of additional ablation in PVs showing acute reconnection after adenosine administration.[17] The results of this trial will help us to understand whether or not this strategy improves arrhythmia-free survival.

Transient reconnection after successful endocardial PV isolation, has been described to occur in up to 35% of the PVs after the use of adenosine.[18] To the best of our knowledge, no study has assessed the effects of adenosine administration after epicardial PV isolation in a hybrid AF ablation setting. In our series of patients, only one single PV (1%) showed dormant conduction. In this particular patient, it was very difficult to guide the bipolar RF clamp completely around the left PVs. The very upper part of the antrum of the left superior PV (junction with the LA roof) never got in between the jaws of the clamp. This might explain the fact why it was not possible to create a completely transmural lesion epicardially at this specific spot and the apparent entrance block of this PV when checking with the endocardial lasso catheter as a result of incomplete injury. The fact that epicardial PV isolation seems to result in significantly less dormant conduction, might be explained by the greater ability to create completely transmural lesions compared to endocardial energy sources. The epicardial application of bipolar and bilateral RF energy, as used in this series, overcomes the heat sink by clamping the tissue and excluding the effect of the circulating blood on ablation, which seems to result in more persistent lesions.[19, 20]

Study limitations

The small number of patients in this single-center study prevents definitive conclusions. However, future larger studies may confirm our results. It remains unclear whether additional endocardial application of RF at sites showing acute reconnection, improve long-term results. Prolonging the waiting time after initial epicardial PV isolation, may increase the number of PVs with acute reconnection after adenosine. Although none of the PVs appeared to be isolated in any of the patients with a previous catheter ablation procedure, it cannot be excluded that previous catheter ablation favorably influenced the results.

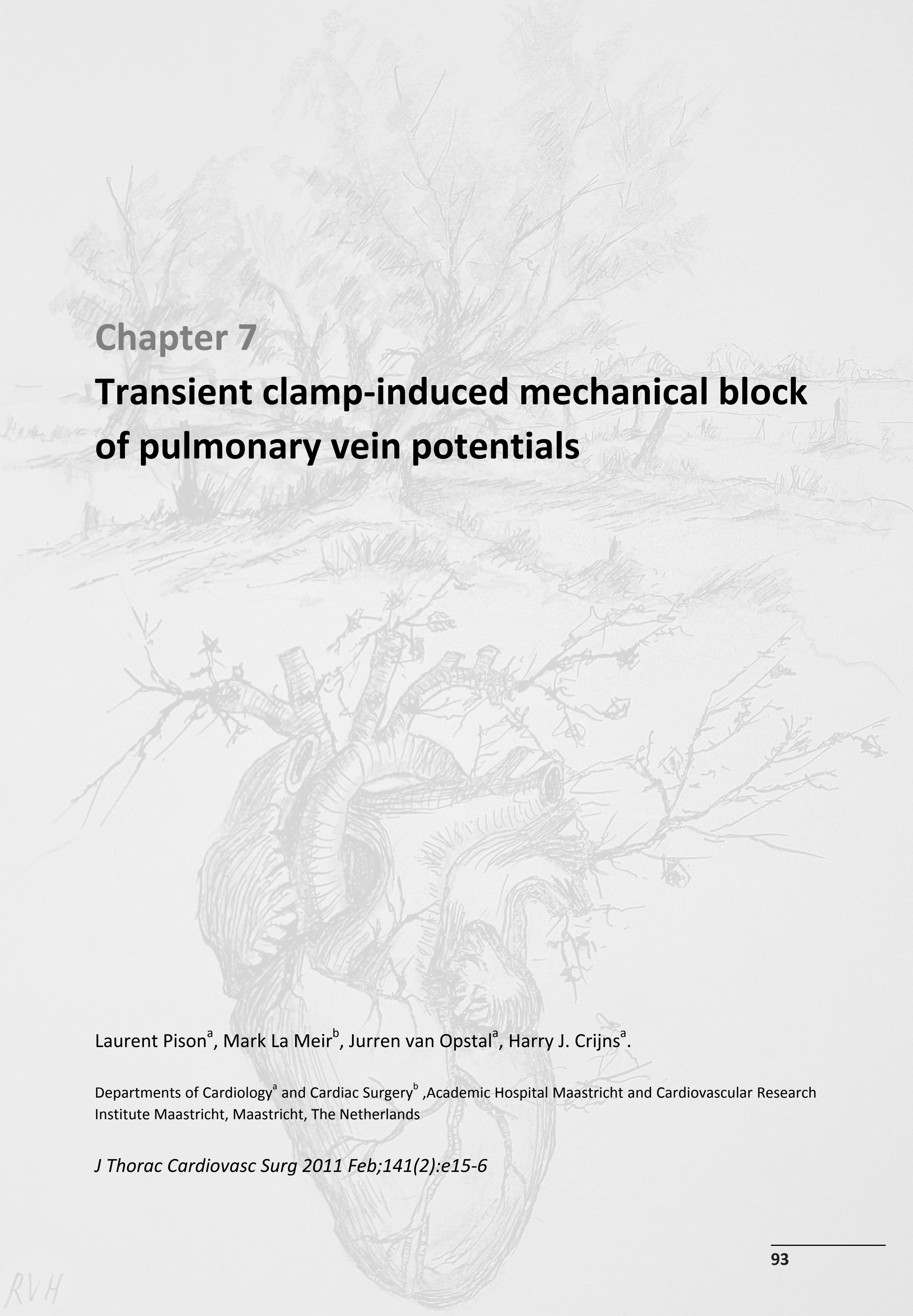
Conclusions

Adenosine administration during hybrid ablation of AF to test dormant PV conduction, is feasible and safe. After epicardial PV isolation, adenosine unmasks dormant conduction in 1% of the PVs.

References

1. Haissaguerre M, Jais P, Shah DC, Takahashi A, Hocini M, Quiniou G, Garrigue S, Le Mouroux A, Le Metayer P, Clementy J. Spontaneous initiation of atrial fibrillation by ectopic beats originating in the pulmonary veins. *The New England journal of medicine*. 1998;339:659-666
2. Callans DJ, Gerstenfeld EP, Dixit S, Zado E, Vanderhoff M, Ren JF, Marchlinski FE. Efficacy of repeat pulmonary vein isolation procedures in patients with recurrent atrial fibrillation. *Journal of cardiovascular electrophysiology*. 2004;15:1050-1055
3. Thomas SP, Sanders P. Catheter ablation for atrial fibrillation. *Heart, lung & circulation*.21:395-401
4. McLellan AJ, Kumar S, Smith C, Morton JB, Kalman JM, Kistler PM. The role of adenosine following pulmonary vein isolation in patients undergoing catheter ablation for atrial fibrillation: A systematic review. *Journal of cardiovascular electrophysiology*. 2013;24:742-751
5. Arentz T, Macle L, Kalusche D, Hocini M, Jais P, Shah D, Haissaguerre M. "Dormant" pulmonary vein conduction revealed by adenosine after ostial radiofrequency catheter ablation. *Journal of cardiovascular electrophysiology*. 2004;15:1041-1047
6. Miyazaki S, Kuwahara T, Kobori A, Takahashi Y, Takei A, Sato A, Isobe M, Takahashi A. Impact of adenosine-provoked acute dormant pulmonary vein conduction on recurrence of atrial fibrillation. *Journal of cardiovascular electrophysiology*. 2012;23:256-260
7. Calkins H, Kuck KH, Cappato R, Brugada J, Camm AJ, Chen SA, Crijns HJ, Damiano RJ, Jr., Davies DW, DiMarco J, Edgerton J, Ellenbogen K, Ezekowitz MD, Haines DE, Haissaguerre M, Hindricks G, Iesaka Y, Jackman W, Jalife J, Jais P, Kalman J, Keane D, Kim YH, Kirchhof P, Klein G, Kottkamp H, Kumagai K, Lindsay BD, Mansour M, Marchlinski FE, McCarthy PM, Mont JL, Morady F, Nademanee K, Nakagawa H, Natale A, Nattel S, Packer DL, Pappone C, Prystowsky E, Raviele A, Reddy V, Ruskin JN, Shemin RJ, Tsao HM, Wilber D, Heart Rhythm Society Task Force on C, Surgical Ablation of Atrial F. 2012 hrs/ehra/ecas expert consensus statement on catheter and surgical ablation of atrial fibrillation: Recommendations for patient selection, procedural techniques, patient management and follow-up, definitions, endpoints, and research trial design: A report of the heart rhythm society (hrs) task force on catheter and surgical ablation of atrial fibrillation. Developed in partnership with the european heart rhythm association (ehra), a registered branch of the european society of cardiology (esc) and the european cardiac arrhythmia society (ecas); and in collaboration with the american college of cardiology (acc), american heart association (aha), the asia pacific heart rhythm society (aphrs), and the society of thoracic surgeons (sts). Endorsed by the governing bodies of the american college of cardiology foundation, the american heart association, the european cardiac arrhythmia society, the european heart rhythm association, the society of thoracic surgeons, the asia pacific heart rhythm society, and the heart rhythm society. *Heart rhythm : the official journal of the Heart Rhythm Society*. 2012;9:632-696 e621
8. Pison L, La Meir M, van Opstal J, Blaauw Y, Maessen J, Crijns HJ. Hybrid thoracoscopic surgical and transvenous catheter ablation of atrial fibrillation. *Journal of the American College of Cardiology*. 2012;60:54-61
9. Ouyang F, Bansch D, Ernst S, Schaumann A, Hachiya H, Chen M, Chun J, Falk P, Khanedani A, Antz M, Kuck KH. Complete isolation of left atrium surrounding the pulmonary veins: New insights from the double-lasso technique in paroxysmal atrial fibrillation. *Circulation*. 2004;110:2090-2096
10. Verma A, Kilicaslan F, Pisano E, Marrouche NF, Fanelli R, Brachmann J, Geunther J, Potenza D, Martin DO, Cummings J, Burkhardt JD, Saliba W, Schweikert RA, Natale A. Response of atrial fibrillation to pulmonary vein antrum isolation is directly related to resumption and delay of pulmonary vein conduction. *Circulation*. 2005;112:627-635
11. Medi C, Sparks PB, Morton JB, Kistler PM, Halloran K, Rosso R, Vohra JK, Kumar S, Kalman JM. Pulmonary vein antral isolation for paroxysmal atrial fibrillation: Results from long-term follow-up. *Journal of cardiovascular electrophysiology*. 2011;22:137-141
12. Vogt J, Heintze J, Gutleben KJ, Muntean B, Horstkotte D, Nolker G. Long-term outcomes after cryoballoon pulmonary vein isolation: Results from a prospective study in 605 patients. *Journal of the American College of Cardiology*. 2013;61:1707-1712

13. Reddy VY, Neuzil P, Themistoclakis S, Danik SB, Bonso A, Rossillo A, Raviele A, Schweikert R, Ernst S, Kuck KH, Natale A. Visually-guided balloon catheter ablation of atrial fibrillation: Experimental feasibility and first-in-human multicenter clinical outcome. *Circulation*. 2009;120:12-20
14. Kumar S, Morton JB, Lee J, Halloran K, Spence SJ, Gorelik A, Hepworth G, Kistler PM, Kalman JM. Prospective characterization of catheter-tissue contact force at different anatomic sites during antral pulmonary vein isolation. *Circulation. Arrhythmia and electrophysiology*. 2012;5:1124-1129
15. Datino T, Macle L, Qi XY, Maguy A, Comtois P, Chartier D, Guerra PG, Arenal A, Fernandez-Aviles F, Nattel S. Mechanisms by which adenosine restores conduction in dormant canine pulmonary veins. *Circulation*. 2010;121:963-972
16. Kistler PM, Ho SY, Rajappan K, Morper M, Harris S, Abrams D, Sporton SC, Schilling RJ. Electrophysiologic and anatomic characterization of sites resistant to electrical isolation during circumferential pulmonary vein ablation for atrial fibrillation: A prospective study. *Journal of cardiovascular electrophysiology*. 2007;18:1282-1288
17. Macle L, Khairy P, Verma A, Weerasooriya R, Willems S, Arentz T, Novak P, Veenhuyzen G, Scavee C, Skanes A, Puererfellner H, Jais P, Khaykin Y, Rivard L, Guerra PG, Dubuc M, Thibault B, Talajic M, Roy D, Nattel S, Investigators AS. Adenosine following pulmonary vein isolation to target dormant conduction elimination (advice): Methods and rationale. *The Canadian journal of cardiology*. 2012;28:184-190
18. Tritto M, De Ponti R, Salerno-Uriarte JA, Spadacini G, Marazzi R, Moretti P, Lanzotti M. Adenosine restores atrio-venous conduction after apparently successful ostial isolation of the pulmonary veins. *European heart journal*. 2004;25:2155-2163
19. Prasad SM, Maniar HS, Schuessler RB, Damiano RJ, Jr. Chronic transmural atrial ablation by using bipolar radiofrequency energy on the beating heart. *The Journal of thoracic and cardiovascular surgery*. 2002;124:708-713
20. Bugge E, Nicholson IA, Thomas SP. Comparison of bipolar and unipolar radiofrequency ablation in an in vivo experimental model. *European journal of cardio-thoracic surgery : official journal of the European Association for Cardio-thoracic Surgery*. 2005;28:76-80; discussion 80-72



Chapter 7

Transient clamp-induced mechanical block of pulmonary vein potentials

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A hybrid atrial fibrillation (AF) ablation procedure (combining an endocardial and epicardial approach under general anesthesia) was performed in a 68-year-old man with symptomatic paroxysmal AF of 4 years duration. The patient also had hypertension and prolapse of the mitral valve. His medication consisted of flecainide, perindopril, and warfarin. Flecainide was stopped 5 days before the procedure. Normal left ventricular (LV) systolic function, an enlarged left atrium (LA) with a volume of 99 mL (normal<61 mL), minimal LV hypertrophy, and a mild degree of mitral regurgitation were observed on transthoracic echocardiography.

Clinical Summary

A His and coronary sinus (CS) catheter were inserted via the left groin. After transseptal puncture guided by transesophageal echocardiography, a long sheath was advanced from the right groin into the LA and the patient was fully heparinized. After placing a circular mapping catheter (Lasso; Biosense Webster Inc, Diamond Bar, Calif) at the ostium of the pulmonary veins (PVs) one by one, we observed the presence of pulmonary vein potentials (PVP) in sinus rhythm in the right PVs and during pacing from the distal CS catheter in the left PVs. Pacing from the Lasso catheter revealed locale capture in each PV with conduction to the LA. Via a bilateral thoracoscopic approach, we paced from the epicardial side of each PV with a 4-mm tip quadripolar catheter (Biosense Webster Inc) at the level of the Lasso catheter and were able to demonstrate locale capture with conduction to the LA.

After placing the Lasso catheter out of the left superior PV (LSPV), we placed a bipolar radiofrequency (RF) clamp (Atricure Inc, West Chester, Ohio) around the two left PVs. We closed the clamp for 1 minute without application of RF to evaluate whether this maneuver would result in conduction block. After the clamp was opened, the Lasso catheter was replaced at the ostium of the LSPV (Fig 1). We noticed dissociated PVPs, wich prove exit and entrance block. Pacing sequentially from the epicardial and endocardial side of the LSPV resulted in local capture (PVPs on the Lasso catheter) with no conduction to the LA. We did not use adenosine to demonstrate dormant PV conduction. Twenty-one minutes after having removed the clamp, electrical conduction from LA to LSPV reappeared on the Lasso catheter with a long interval between the far-field LA potential and the PVP (Fig. 2), indicating slow conduction from LA to LSPV. To isolate the PVs, we repositioned and closed the clamp around the left PVs and applied bipolar RF. The right PVs were isolated in the same way using this device. After the last application of bipolar RF, we waited more than 30 minutes. During this waiting time the cavo-tricuspid isthmus was ablated endocardially using a 3.5 mm tip catheter (ThermoCool; Biosense-Webster Inc). We were then able to demonstrate bidirectional block both at the level of the PVs from the endocardial and epicardial sides. This finding was also confirmed during infusion of isoproterenol.

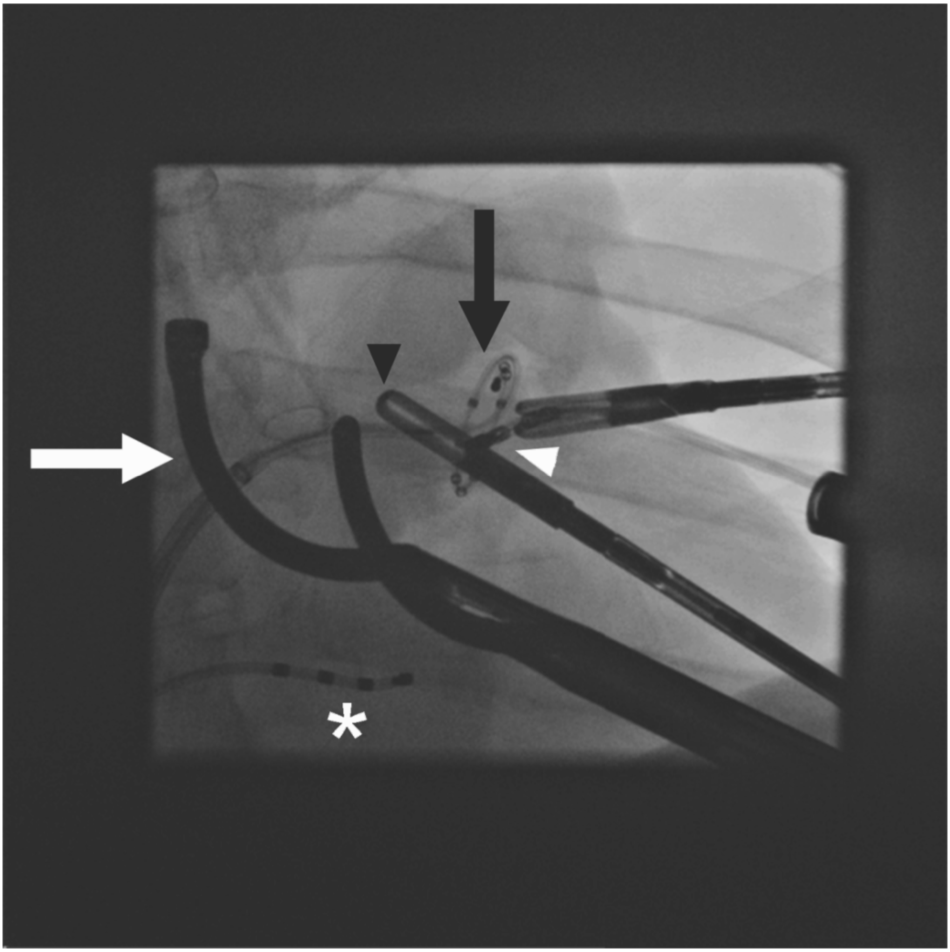


Figure 1. Fluoroscopic image shows the opened bipolar radiofrequency clamp (white arrow) placed epicardially at the antrum of the left pulmonary veins, the endocardial circular mapping catheter (black arrow) at the ostium of the left superior pulmonary vein (LSPV), the quadripolar catheter on the epicardial surface of the LSPV (white arrowhead), a His catheter (asterisk) and a surgical forceps (black arrowhead).

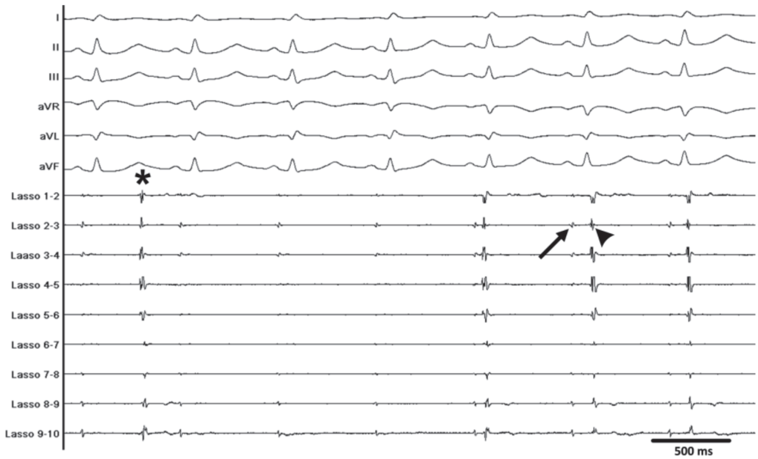


Figure 2. A circular mapping catheter at the ostium of the left superior pulmonary vein, registers a local left pulmonary vein potential that is dissociated from the left atrium during sinus rhythm (asterisk). A few seconds later, conduction from the left atrium to the left superior pulmonary vein reappears: pulmonary vein potentials (arrowhead) are inscribed late after far-field left atrial activity (arrow).

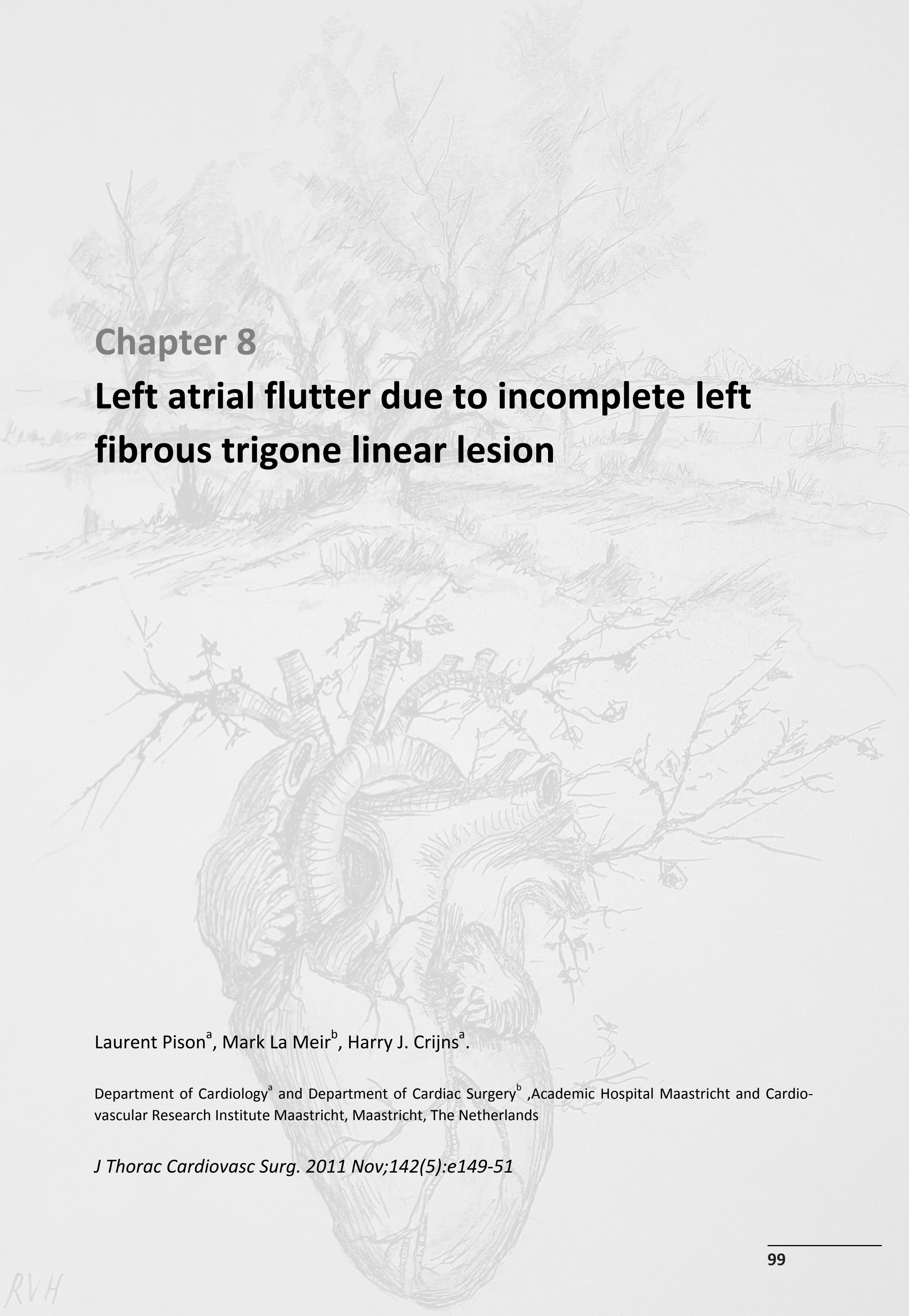
Conduction block over anatomic structures sometimes occurs during manipulation of catheters in the cardiac chambers. This conduction block is ascribed to mechanical trauma and is referred to as “catheter-induced trauma.” Catheter-induced trauma has been reported in the atrioventricular node, His bundle, accessory pathways, and others.[1,2] This case report demonstrates for the first time how clamp-induced pressure or trauma from the epicardium leads to transient block of PVPs. This finding is of paramount importance for cardiac surgeons and electrophysiologists involved in the field of surgical or hybrid AF ablation. As stated in the HRS/EHRA/ECAS Expert Consensus Statement, ablation strategies that target the PVs or PV antrum are the cornerstone for most AF ablation procedures, but if the PVs are targeted, complete electrical isolation should be the goal.[3] Benussi et al described recovery of PV conduction in 15% of patients 3 weeks after epicardial ablation with a bipolar RF clamp.[4] They suggest that small gaps around the PV antrum can be masked by edema owing to heart trauma and that resolution of swelling during recovery of ablation may allow for PV reconnection. Our case clearly illustrates this finding because trauma (closing of the clamp) leads to transient isolation of the PV.

Conclusions

A clinical implication of this case report is that, because of unnoticed mechanical block, epicardial ablation should be performed on all PVs even if no PVPs are seen.

References

1. Belhassen B, Viskin S, Fish R, Glick A, Glikson M, Eldar M. Catheter-Induced Mechanical Trauma to Accessory Pathways during Radiofrequency Ablation: Incidence, Predictors and Clinical Implications. J Am Coll Cardiol 1999;33:767-74.
2. Topolski I, Rogowski O, Glick A, Viskin S, Eldar M, Belhassen B. Catheter-Induced Mechanical Trauma to Fast and Slow Pathways during Radiofrequency Ablation of Atrioventricular Nodal Reentry Tachycardia: Incidence, Predictors and Clinical Implications. PACE 2007;30:1233-41.
3. Calkins H, Brugada J, Packer DL, Cappato R, Chen SA, Crijns HJ, et al. HRS/EHRA/ECAS expert consensus statement on catheter and surgical ablation of atrial fibrillation: recommendations for personnel, policy, procedures, and follow-up: a report of the Heart Rhythm Society Task Force on Catheter and Surgical Ablation of Atrial Fibrillation. Heart Rhythm. 2007;4:816–861.
4. Benussi S, Galanti A, Zerbi V, Privitera Y, Iafelice I, Alfieri O. Electrophysiologic efficacy of irrigated bipolar radiofrequency in the clinical setting. J Thorac Cardiovasc Surg 2010;139:1131-1136.



Chapter 8

Left atrial flutter due to incomplete left fibrous trigone linear lesion

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A 59-year-old man underwent a minimally invasive thoracoscopic surgical ablation procedure for symptomatic persistent atrial fibrillation (AF) of 7 years duration. His medication consisted of propafenon, metoprolol, and warfarin. Normal left ventricular systolic function and enlarged left atrium with a volume of 86 mL (normal < 66 mL) were observed on transthoracic echocardiography. Computed tomography of the coronary arteries revealed no significant stenosis.

During this procedure the pulmonary veins (PV) were isolated in pairs with a bipolar radiofrequency clamp (Atricure Inc, West Chester, OH). A roofline connecting both superior PVs and an inferiorline from one inferior PV to the other were made using a bipolar radiofrequency linear pen device (Coolrail, Atricure Inc, West Chester, OH). In this way we created a so-called box lesion. Due to ongoing AF, a left fibrous trigone line was created using a bipolar radiofrequency pen device (Isolator Pen, Atricure, West Chester, OH). This connecting lesion is placed from the left fibrous trigone at the anterior mitral valve annulus across the anterior dome of the atrium to the roofline. Because the patient remained in AF at the end of the procedure, he was electrically cardioverted. After an uneventful postoperative recovery, he was discharged on warfarine and his preoperative antiarrhythmic drugs (AAD) regimen.

Initially the patient remained asymptomatic and 7 days Holter at 3 and 6 months revealed continuous sinus rhythm. Warfarine and AADs were stopped. Seven months after the procedure, a symptomatic left atrial flutter was documented (Figure 1, A). Rate controle with metoprolol was initiated in combination with warfarine. After informed consent, the patient was scheduled for an electrophysiological study.

After transseptal puncture and placement of a His and coronary sinus catheter, an activation and endocardial voltage map of the tachycardia was made using a three-dimensional electroanatomical mapping system (CARTO, Biosense-Webster, Diamond Bar, CA) (Figure 2). In combination with concealed entrainment mapping, we were able to confirm a counterclock-wise left atrial flutter evolving around the mitral valve annulus. By placing a properly sized circular mapping catheter (Lasso, Biosense Webster Inc., Diamond Bar, CA) at the antrum of the PVs, complete isolation could be proved during tachycardia by the absence of PV potentials. Also the box appeared to be isolated as we detected no nearfield signals on the Lasso catheter placed at the posterior wall of the LA. At the endocardial level of the left fibrous trigone line, the voltage map revealed a line of low voltages but no scar extending from the mitral valve annulus towards the medial aspect of the roof line. This indicated that the left fibrous trigone linear lesion made during surgical ablation procedure was not transmural. Using a 3.5-mm-tip catheter (ThermoCool, Biosense Webster Inc., Diamond Bar, CA) we ablated all the remnant low voltages along this line starting at the mitral valve annulus (Figure 2). During ablation we saw a gradual increase in the tachycardia cycle length and connection of the endocardial linear lesion with the roofline resulted in conversion to sinus rhythm (Figure 1, B and C).

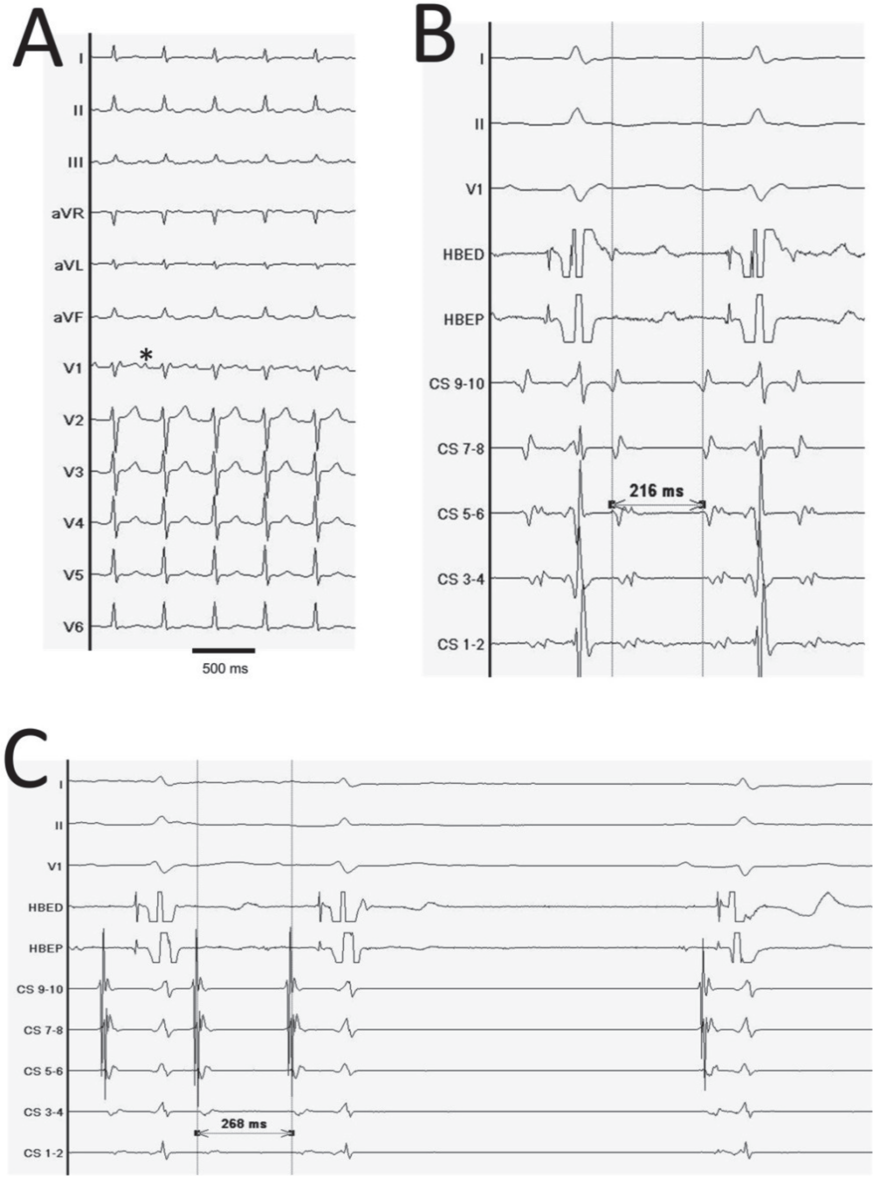


Figure 1. (A) The 12-lead ECG shows an atrial flutter with positive flutter waves in lead V1 suggesting a left atrial origin. **(B)** His (HBE) and coronary sinus (CS) electrocardiogram showing a tachycardia cycle length of 216 msec. **(C)** During endocardial ablation the tachycardia cycle length increased gradually to a maximum of 268 msec and then converted to sinus rhythm at the moment the endocardial linear lesion connected to the roofline.

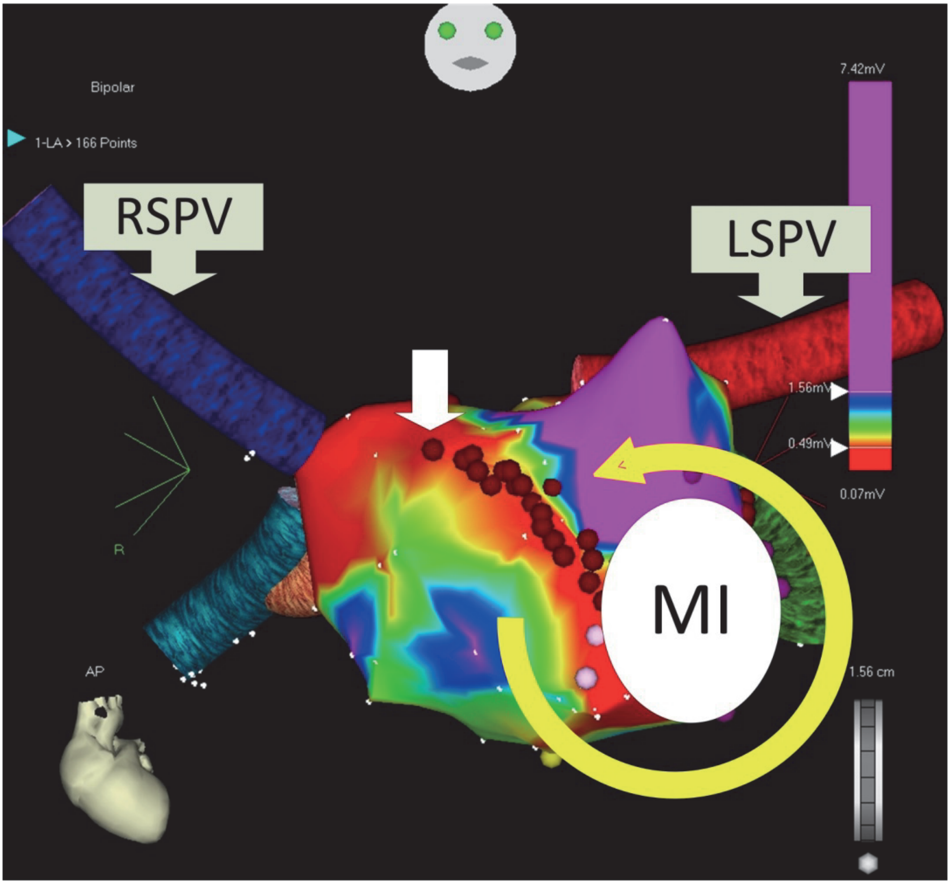
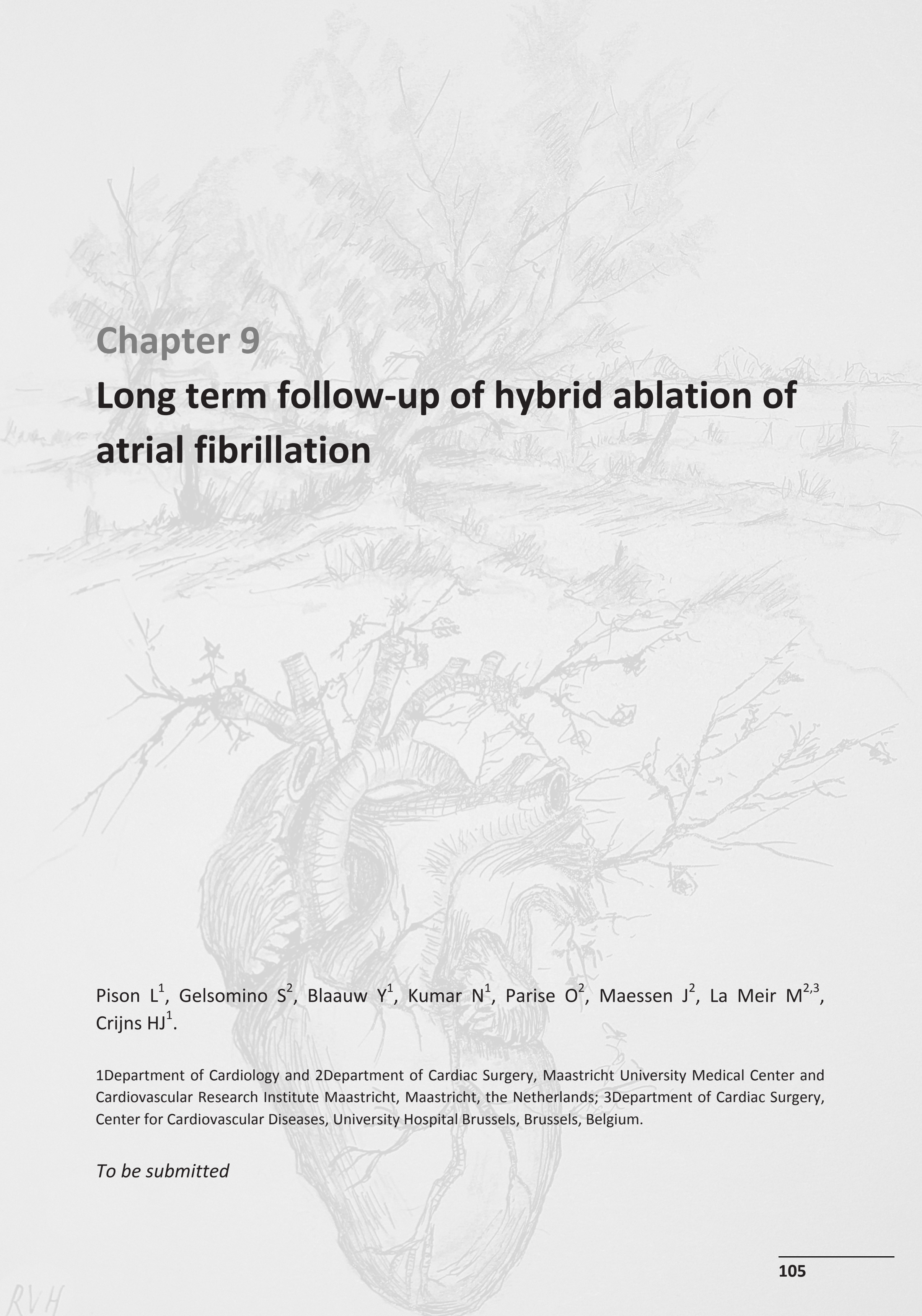


Figure 2. Voltage map of the left atrium The clinical tachycardia was a counterclock-wise left atrial flutter evolving around the mitral annulus (MI) (yellow arrow). By ablating al the remnant endocardial zones of low voltages at the left fibrous trigone line (red dots), we interrupted surviving strands of atrial tissue hereby creating a linear lesion extending from the MI to the medial aspect of the roofline (white arrow) resulting in gradual increase of the tachycardia cycle length and finally conversion to sinus rhythm. LSPV = left superior pulmonary vein, RSPV = right superior pulmonary vein.

Bilateral video-assisted thoracoscopic PV isolation is a safe, beating-heart approach for curative surgical treatment of AF.[1] Linear lesions are known to improve outcome of catheter ablation in patients with persistent atrial fibrillation.[2] The left fibrous trigone line was introduced by Edgerton et al.[3] This linear lesion serves as an alternative to the endocardial mitral isthmus line extending from the left inferior PV to the mitral valve annulus. The creation of a completely transmural left fibrous trigone line can be hampered by the presence of epicardial fat. Not completely transmural lesions, exhibit zones of low voltages and conduction slowing and can hereby become pro-arrhythmic.[4] In our case, an incomplete left fibrous trigone line resulted in a left atrial flutter. Most of those iatrogenic arrhythmias are very symptomatic. In order to prevent as much as possible such reentry circuits to occur, it is of paramount importance to proof complete transmurality of each deployed linear lesion. This can effectively be done using an epicardial approach or a combined simultaneous thoracoscopic surgical and transvenous catheter procedure.

References

1. Wolf RK, Schneeberger EW, Osterday R, Miller D, Merrill W, Flege JB, et al. Video-assisted bilateral pulmonary vein isolation and left atrial appendage exclusion for atrial fibrillation. *J Thorac Cardiovasc Surg* 2005;130:797-802
2. Willems S, Klemm H, Rostock T, Brandstrup B, Ventura R, Steven D, et al. Substrate modification combined with pulmonary vein isolation improves outcome of catheter ablation in patients with persistent atrial fibrillation: a prospective randomized comparison. *European Heart Journal* 2006;27:2871-2878.
3. Edgerton JR, Jackman WM, Mack MJ. A new epicardial lesion set for minimal access left atrial maze: the Dallas lesion set. *Annals of Thoracic Surgery* 2009;88:1655-1657.
4. Sawhney N, Anousheh R, Chen W, Feld GK. Circumferential pulmonary vein ablation with additional linear ablation results in an increased incidence of left atrial flutter compared with segmental pulmonary vein isolation as an initial approach to ablation of paroxysmal atrial fibrillation. *Circulation Arrhythmia and Electrophysiology* 2010;3(3):243-248.
5. Pison L, La Meir M, Maessen J, Crijns HJ. Hybrid thoracoscopic surgical and transvenous catheter ablation of AF, towards single procedure ablation of longstanding AF. *Heart Rhythm* 2010;7 Suppl 5:S-398.



Chapter 9

Long term follow-up of hybrid ablation of atrial fibrillation

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To be submitted

Introduction

The cornerstone of atrial fibrillation (AF) ablation is isolation of the pulmonary veins (PV).[1]

In patients with paroxysmal AF, success rates of catheter ablation (CA) targeting the PVs exceed 80%.[2] To achieve acceptable results in patients with persistent AF, one needs to combine PV isolation with linear lesions and/or ablation of complex fractionated atrial electrograms.[3] One of the major weaknesses of endocardial catheter based ablation techniques, is their inability to guarantee longlasting transmurality of the lesions. This is the reason why recurrent AF after endocardial ablation, is often associated with PV reconnection.[4] Modern surgical AF ablation techniques, on the other hand, are less confronted with incomplete lesions but they lack the ability to define the specific properties of the underlying atrial electrical substrate in order to customize the subsequent ablation strategy. We therefore developed a hybrid approach that combines a transvenous endocardial and thoracoscopic epicardial approach in a single procedure in order to overcome their mutual shortcomings.[5] In this study we report the long-term follow-up results of this hybrid procedure

Methods

Study population

Fifty-six consecutive patients with symptomatic AF underwent hybrid thoracoscopic surgical and transvenous CA with follow-up of at least 2 years. Definitions of paroxysmal, persistent, and longstanding persistent AF, success and failure of ablation, and follow-up monitoring were based on the Heart Rhythm Society, European Heart Rhythm Association, and European Cardiac Arrhythmia Society consensus statement.[1] Selection criteria for this procedure were previously failed CA, failure of at least one antiarrhythmic drug (AAD), left atrial (LA) volume ≥ 29 ml/m2, persistent or longstanding persistent AF, or patient preference for a hybrid procedure instead of a percutaneous approach. Eighteen patients (32%) had prior CA for AF and 11 (20%) for atrial flutter (AFL). The preoperative work-up consisted of transthoracic echocardiography, cardiac computed tomography, and pulmonary function testing.

Hybrid procedure

The hybrid ablation procedure was performed as described in detail elsewhere.[5] Briefly, 1 working port and 2 camera ports were inserted on both sides of the thorax. Subsequently, the pericardium and the transverse and oblique sinuses were opened during selective lung ventilation. Via the femoral venous approach, a His bundle (St. Jude Medical, St. Paul, Minnesota) and coronary sinus (CS) catheter (Medtronic, Minneapolis, Minnesota) were placed under fluoroscopy, and transseptal puncture was performed with a long 8-F sheath (SL0, St. Jude Medical) into the LA, followed by heparinization. The pulmonary veins (PV) were mapped with a circular mapping catheter (Lasso, Biosense Webster, Diamond Bar, California). Antral isolation of the right and left PVs as a pair was performed with a bipolar radiofrequency (RF) clamp (Atricure, West Chester, Ohio). The end point for PV ablation was entrance and exit block. Selective ablation of the ganglionic plexi (GP) was not undertaken. In order to avoid bilateral sequential lung deflation in patients with severe chronic obstructive pulmonary disease , we performed thoracoscopic epicardial isolation of the PVs only on the right, and the left PVs were isolated endocardially using a cryothermal energy balloon catheter (Arctic Front; Cryocath, Montreal, Quebec City, Canada). In the case of normal sinus rhythm (NSR) after PV isolation, re-induction of AF was attempted by burst pacing in the coronary sinus. AF was considered inducible if it lasted more than 1 min. If AF became noninducible, isoproterenol was infused at rates of 10 to 30 µg/min. If AF had not terminated or still was inducible, linear lesions were created. A roof line (connecting both superior PVs) and an inferior line (connecting both inferior PVs) were made epicardially using a bipolar RF pen or linear pen device (Isolater Pen and Coolrail; Atricure). These two linear lesions, in combination with bilateral antral PV isolation, result in electrical isolation (bidirectional block) of the posterior LA (box lesion). Any conduction gap in these epicardial linear lesions was ablated endocardially with a 3.5-mm-tip catheter (Thermo-Cool; Biosense Webster). A left isthmus line was made in patients developing a mitral isthmus dependent left AFL during the procedure. The line was created epicardially using the bipolar RF pen device, starting from the ablation line on the antrum of the left inferior PV toward and crossing the coronary sinus. All patients needed endocardial touch-up ablation to reach bidirectional block. If the patient was known to have typical AFL or if this arrhythmia occurred during the procedure, the cavotricuspid isthmus (CTI) was ablated endocardially. If the right atrium was dilated on transthoracic echocardiography, 2 additional epicardial ablation lines were performed: one encircling the superior caval vein and the other connecting both caval veins. Patients still in AF after PV isolation and deployment of linear lesions, underwent electrical cardioversion. The left atrial appendage was excluded using a clipping device (Atriclip; Atricure) in 18 (32%) patients. Finally, The pericardium was approximated with a stitch, and a chest tube was placed in both pleural cavities. Six hours thereafter, low–molecular weight heparin was started. Acenocoumarol was reinitiated on the second post-operative day and the pre-operative AAD regimen as soon as possible. If the 6-month monitoring visit confirmed the absence of atrial arrhythmia, acenocoumarol and AADs were stopped.

Long-term follow-up

Any symptomatic patient not in NSR was cardioverted before the 3-month follow-up visit. Two patients had a pacemaker, which was used for monitoring. The remaining patients underwent 7-day continuous Holter monitoring at 3, 6, 9, 12, 24, 36 and 48 months. If 7-day Holter monitoring was not available, patients underwent at least 24-h Holter monitoring. According to current guidelines, success was defined as no episode of AF, AFL, or any atrial tachycardia (AT) lasting more than 30 seconds off AAD after the 3-month blanking period. Twelve (21%) patients developed recurrent supraventricular arrhythmia. They were offered the options of AAD or invasive electrophysiology study (EPS) and RF ablation.

Electrophysiological study

Patients were brought to the laboratory in a fasting state, and all AADs were stopped for five days, except for amiodarone. Multielectrode catheters were advanced and positioned at the bundle of His and in the CS using fluoroscopy. Double transseptal puncture was performed in all patients using transesophageal echocardiography and fluoroscopic guidance. After the last transseptal puncture, the patient underwent heparinization (1,000 U heparin per 10 kg body weight and a heparin infusion), with activated clotting time > 300 seconds. An angiogram of the LA was performed in order to visualize the ostium of the PVs. Subsequently, an electro-anatomical map (EAM) of the LA was created using the EnSite Velocity (St. Jude Medical) or Carto 3 (Biosense Webster) system. A circular mapping catheter was positioned sequentially at each PV ostium to determine whether the PV was still electrically isolated. Atrial pacing was performed from multiple sites at a cycle length of 15 to 20 ms less than the tachycardia cycle length in the case of AFL. Sites with concealed entrainment and where the post-pacing interval minus tachycardia cycle length was < 30 ms, were considered to be part of the flutter circuit.

Ablation

In the event of a macro-reentry AFL, the critical isthmus was localized using the information of the EAM in combination with entrainment mapping. RF ablation was performed at this site using a 3.5-mm-tip RF catheter (Thermo-Cool; Biosense Webster) until conversion to NSR and bidirectional block across this lesion was achieved. For patients presenting with AF or focal/micro-reentry AT, isolation of the PVs was assessed first with a circular mapping catheter. If one or more of the PVs showed reconnection, re-isolation was performed using the same RF catheter as described earlier. The endpoint for PV re-isolation was entrance and exit block. For focal or micro-reentry ATs originating outside the PVs, an EAM was performed to localize the focus. Ablation was performed with RF and the endpoint was conversion to NSR.

Statistics

Data were retrospectively entered into a database. Statistical analysis was performed using SPSS version 20.0 (SPSS, Inc., Chicago, Illinois). Continuous variables are summarized with means and standard deviations or as median and interquartile range. Outcomes are displayed using Kaplan-Meier plots. Any episode of AF, AFL, or AT lasting more than 30 seconds detected after the 3-month postprocedural period by electrocardiography, pacemaker interrogation, or 7-day, 48-h, or 24-h continuous Holter monitoring performed at 6, 9, 12, 24, 36, and 48 months was considered failure.

Results

Perioperative results

Fifty-six patients underwent hybrid procedures between May 29, 2008, and September 5, 2011. Patients' baseline characteristics are shown in Table 1. Twenty-five patients had persistent AF, and 2 had longstanding persistent AF. Eight-teen patients had at least 1 previous CA for AF and in only one patient the PVs appeared to be isolated after this. No patient had undergone previous cardiothoracic surgery. Twenty-five (45%) patients were in AF at the start of the procedure. The mean follow-up period was 1084±363 days (range: 90 to 1826 days).

Table 1. Baseline characteristics (n=56)

Demographic variables	
- Age at inclusion (yrs)	59,2±9,3 (38-78)
- Male gender (%)	71
Medical history	
- Type of atrial fibrillation (%)	
Paroxysmal	51
Persistent	45
Long-standing persistent	4
- History of atrial fibrillation (months)	48 [24-84]
- Structural heart disease (%)	
Ischemic	13
Left ventricular hypertrophy	33
Valvular heart disease	0
Idiopathic dilated cardiomyopathy	7
- Left ventricular ejection fraction (%)	59±8 (36-70)
- LA diameter (mm)/volume (cc)	44±5 (32-53) / 91±24 (38-162)
- Risk factors for thromboembolism (%)	
Hypertension	39
Diabetes	2
Congestive cardiac failure	5
Prior TIA or stroke	4
- BMI (kg/m^2)	26,9±3,2 (19,7-35,6)
CHA2DS2-VASc score (%)	
- 0	28
- 1	36
- ≥ 2	36
Medical therapy (%)	
- Sotalol	25
- Flecainide	38
- Amiodarone	20
- VKA	92
Ablation therapy (%)	
- Previous AF ablation	32
- Previous AFL ablation	20

Baseline characteristics of all included patients.
Yrs = years, LA = left atrium, TIA = transient ischemic attack, BMI = body mass index, VKA = vitamin K antagonist, AF = atrial fibrillation, AFL = atrial flutter.
Data presented as mean±SD (range) or as median [interquartile range].

In all patients, we achieved block of all the PVs (Figure 1). In 8 patients with severe chronic obstructive pulmonary disease, we performed thoracoscopic epicardial isolation of the PVs only on the right, and the left PVs were isolated endocardially using a cryothermal energy balloon catheter (Arctic Front; Cryocath, Montreal, Quebec City, Canada). In 9 patients, AF was not inducible anymore after PV isolation only. In 2 of them we performed ablation of the CTI because of previously documented typical AFL. In 3 patients, a CTI-dependent counterclockwise right AFL was induced after PV isolation and successfully ablated. In 1 of these 3 patients, we were able to re-induce AF. We deployed a roofline in 45 patients. This resulted in conversion to NSR in 5 patients. In 2 of them it was possible to re-induce AF. In 42 patients a box lesion was created epicardially by deploying an inferiorline. In 6 patients this resulted in a mitral isthmus dependent atrial flutter. In all of these 6 patients we obtained NSR by ablation at the mitral isthmus. In all cases, these lines had to be completed from the endocardium or within the CS. Thirty patients converted to NSR after creation of the box lesion and in 6 of them additional ablation at the CTI was performed (1 patient with inducible right AFL, 3 patients known with right AFL and 2 patients with right AFL after creation of box lesion). After endocardial touch-up in 9 patients (16%), we were able to demonstrate endocardial entrance and exit block in the box during sinus rhythm in 42 patients (75%). In 5 of these 9 patients, there was a gap in the roof line at the junction of the right superior PV with the roof of the LA. One patient had a gap in the lateral portion of the roof line, and 1 patient in the middle of the inferior line. In 1 patient there was a gap in the roof line at the junction of the LA roof with the left superior PV. One patient had a gap at the antrum of the right inferior PV. Four patients were still in AF at the end of the procedure. In 1 of these 4 patients, we deployed an epicardial left fibrous trigone linear lesion. Despite creation of this lesion, AF remained. In these 4 patients, electrical cardioversion was necessary at the end of the procedure because of ongoing AF. Fourteen patients (25%) were discharged on amiodarone and 53 (95%) on acenocoumarol. All patients left the hospital in NSR.

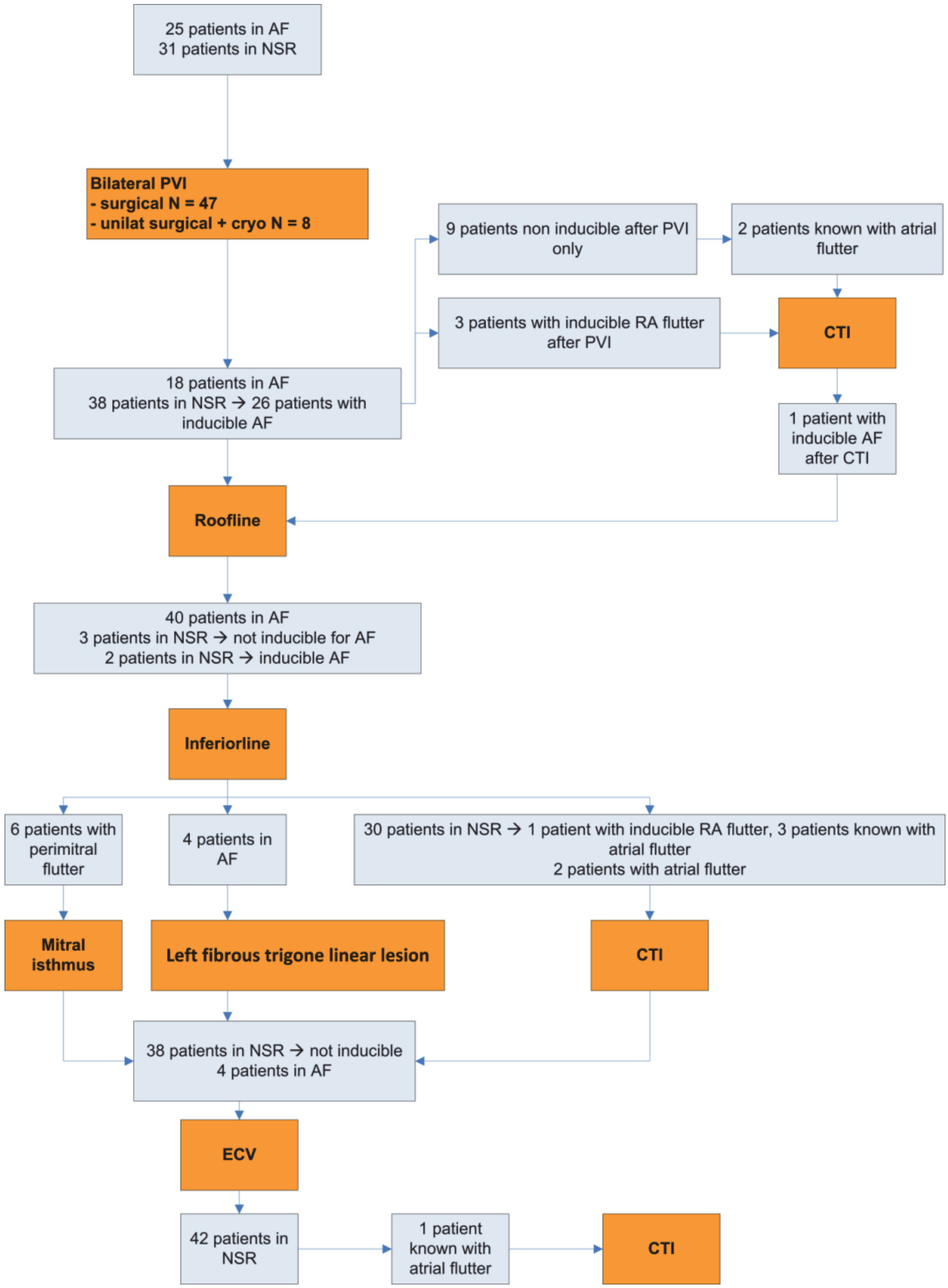


Figure 1. Flow Diagram of the Stepwise Lesion Sets. See text for details.
AF = atrial fibrillation, NSR = normal sinus rhythm, PVI = pulmonary vein isolation, RA = right atrium, CTI = cavotricuspid isthmus, ECV = electrical cardioversion.

Long-term follow-up

Fifty-three (95%) patients reached 2-year follow-up, and three patients (5%) were lost to follow-up (Figure 2). Thirty-seven (66%) patients reached 3-year follow-up and twenty (36%) reached 4-year follow-up. At 2 years, 49 of 53 patients (92%) were in NSR, with no episodes of AF, AFL, or AT lasting longer than 30 seconds on office follow-up, Holter monitoring, or pacemaker interrogation (Table 2). Five (9%) of those 53 patients were on AADs, and 19 (36%) were on acenocoumarol. Thirty-six (97%) of 37 patients were in NSR at 3 years of follow-up. Four (11%) patients were taking AADs and 9 (24%) acenocoumarol. Twenty patients reached the longest follow-up of 4 years. Nineteen (95%) of those patients were in NSR at that time and 4 (20%) were still taking AAD. Five (25%) of 20 patients were on acenocoumarol. Two-year success, defined according to the Heart Rhythm Society, European Heart Rhythm Association, and European Cardiac Arrhythmia Society consensus statement (freedom from AF, AFL, and AT off AADs), was 82% for patients with paroxysmal AF and 88% for patients with non-paroxysmal AF. At 4 year follow-up, 75% of patients with paroxysmal AF and 87% of patients with non-paroxysmal AF were fulfilling these requirements.

A total of 9 (16%) patients underwent CA for recurrence of supraventricular arrhythmia after the hybrid procedure. Eight (15%) of 53 patients by 2 year follow-up had undergone CA and 4 (20%) of 20 patients by 4 year follow-up.

Table 2. Rhythm Assessment

	3 Months	6 Months	12 Months	24Months	36 Months	48 Months
Patients who Completed FU, n	56	55	55	53	37	20
Patients in AF, n(%)	2 (3)	3 (5)	2 (3)	2 (3)	1(2)	1(5)
Patients in AFL, n(%)	2 (3)	2 (3)	0	1(2)	0	0
Patients in AT, n(%)	0	0	0	1(2)	0	0
Patients in NSR, n(%)	52 (93)	49(89)	53(96)	49(92)	36(97)	19(95)
Paroxysmal, n	26	27	28	27	22	12
Persistent, n	24	20	23	20	13	6
LSP, n	2	2	2	2	1	1
Patients in NSR off-AAD, n(%)	7(13)	21(38)	46(84)	45(85)	32(86)	16(80)
Paroxysmal, n	2	10	25	23	19	9
Persistent, n	4	11	20	20	12	6
LSP, n	1	0	1	2	1	1
Patients on AAD, n(%)	49(88)	21(38)	9(16)	5(9)	4(11)	4(20)
Patients on VKA, n(%)	53 (95)	45(81)	24(43)	19(36)	9(24)	5(25)

FU: Follow-up; AF: Atrial Fibrillation; AFL: Atrial Flutter; NSR: Normal sinus rhythm; AAD: Antiarrhythmic drugs; VKA: Vitamin K antagonist.

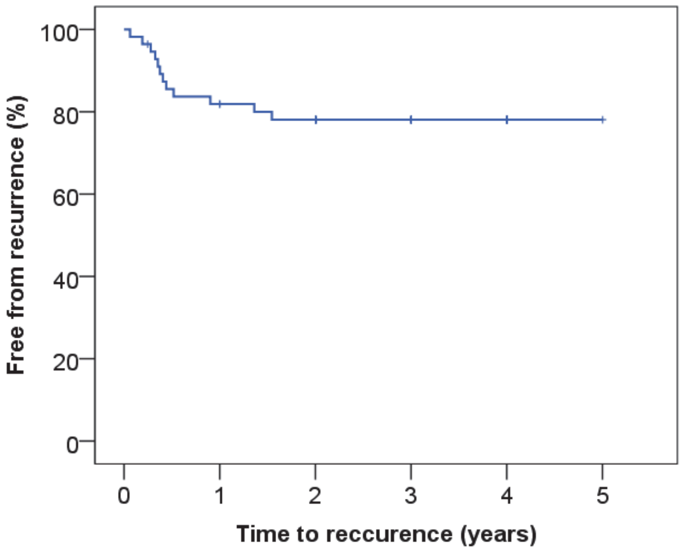


Figure 2. Kaplan-Meier curve showing the arrhythmia free survival after hybrid ablation. See text for details. An event was considered a patient who, at any time after the blanking period, had recurrent supraventricular tachycardia.

Arrhythmia recurrence

Twelve (21%) of 56 patients who underwent hybrid AF ablation procedure, had at least 1 recurrent episode of AF, AFL, or AT lasting longer than 30 seconds on office follow-up, Holter monitoring, or pacemaker interrogation. Of the 12 patients with recurrent supraventricular arrhythmia, 9 chose EPS and RF ablation and 3 medical therapy.

The demographic and clinical characteristics of the 12 patients with arrhythmia recurrence are compared with the 44 patients who underwent hybrid AF ablation without recurrence in Table 3. We analyzed procedural characteristics of patients undergoing hybrid AF ablation and compared patients with and without arrhythmia recurrence (Table 4).

Table 3. Demographic and clinical characteristics of patients with and without arrhythmia recurrence after hybrid AF ablation

	Patients without arrhythmia recurrence (n=44)	Patients with arrhythmia recurrence (n=12)	P value
Age (yrs)	59,3±9,6	58,8±8,6	ns
Male gender (%)	73	67	ns
LVEF (%)	58±8	59±7	ns
AF type (%)			
- Paroxysmal	54	42	ns
- Persistent	41	58	ns
- LS persistent	5	0	ns
AF duration (months)	48 [24-84]	24 [24-84]	ns
LA volume (ml)	89±26	99±16	ns
BMI (kg/m^2)	26,5±3,1	28,1±3,5	ns
Previous catheter ablation (%)	34	25	ns
Hypertension (%)	37	50	ns
CAD (%)	14	8	ns
COPD (%)	9	17	ns

Data presented as mean±SD or as median [interquartile range].
Yrs = years, LVEF = left ventricular ejection fraction, AF = atrial fibrillation, LS = long standing, LA = left atrium, BMI = body mass index, CAD = coronary artery disease, COPD = chronic obstructive pulmonary disease

Table 4. Procedural characteristics of patients with and without recurrent arrhythmia after hybrid AF ablation

	Patients without arrhythmia recurrence (n=44)	Patients with arrhythmia recurrence (n=12)	P value
Lesion set			
- Box lesion (%)	75	75	ns
- Cryo balloon (%)	16	8	ns
- CTI (%)	20	25	ns
- Mitral isthmus (%)	7	25	ns
Endocardial touch-up (%)	20	0	ns
ECV required (%)	0	33	<0.05
LAA exclusion (%)	32	33	ns

CTI = cavotricuspid isthmus ablation, ECV = electrical cardioversion, LAA = left atrial appendage

Electrophysiological study and RF ablation

Table 5 summarizes findings in patients treated with EPS and RF ablation because of arrhythmia recurrence after hybrid AF ablation. The most common recurrent arrhythmia in this group of patients, was left atrial flutter in 4 individuals. In 1 patient this left atrial flutter was characterized by positive flutter waves in lead V1 and a tachycardia cycle length of 216ms. It was successfully treated by re-ablation of an incomplete left fibrous trigone linear lesion (this linear lesion extends from the left fibrous trigone at the anterior mitral valve annulus across the anterior dome of the atrium to the roofline and is also known as the Edgerton line). In the second patient with left atrial flutter the tachycardia cycle length was 200ms and this arrhythmia was successfully ablated at the mitral isthmus (Figure 3). In this patient no mitral isthmus lesion had been deployed previously during the hybrid AF ablation procedure. The left atrial flutter in the third patient was the consequence of an incomplete roofline: we found a micro-reentry circuit located at the junction of the right superior PV with the LA roof (septal side of the roofline)(Figure 4). Application of RF at this spot resulted in conversion to NSR. The last patient with left atrial flutter appeared to have a micro-reentry circuit at the inferior LA (between the mitral valve annulus and the inferior line) (Figure 5) which converted to NSR after focal RF application. Interestingly, in none of those 4 patients with LA flutter there was PV reconnection after the hybrid AF ablation procedure.

Table 5. Baseline and AF characteristics for patients with recurrent supraventricular arrhythmia who underwent EPS and repeat ablation as needed

Patient	AF type	AF duration (months)	Time from surgery to arrhythmia recurrence (days)	Previous CA	Recurrent arrhythmia type	PV reconnection	Ablation sites
1	Pers	84	564	Yes	Left AFL	No	Edgerton line
2	Parox	120	161	No	Parox AF	Yes	Junction right superior PV with roof LA
3	Parox	72	497	No	Parox AF	No	CFAE, AT CS os, re-ablation mitral isthmus
4	Parox	62	119	Yes	Left AFL	No	Mitral isthmus
5	Parox	24	189	No	Pers AF	No	CFAE, redo roofline
6	Pers	72	102	Yes	Left AFL	No	micro-reentry circuit at the junction of the right superior PV with the roof of the LA
7	Pers	24	129	No	Right AFL	No	CTI
8	Pers	24	23	Yes	Left AFL	No	micro-reentry circuit at the inferior LA
9	Pers	12	137	No	Pers AF	Yes	Re-isolation of left superior and inferior PV + right superior PV and ablation AT roof LA

EPS = electrophysiological study, AF = atrial fibrillation, Pers = persistent, Parox = paroxysmal, CA = catheter ablation, AFL = atrial flutter, PV = pulmonary vein, LA = left atrium, CFAE = complex fractionated atrial electrogram, CTI = cavotricuspid isthmus, AT = atrial tachycardia

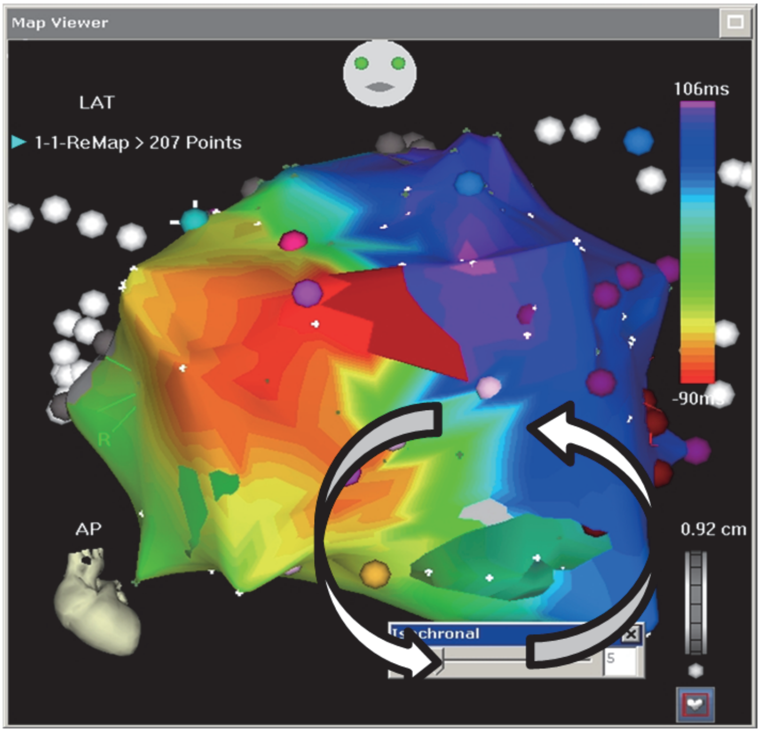


Figure 3. Carto activation map of mitral isthmus dependent left atrial flutter as recurrent arrhythmia after hybrid AF ablation.

Figure 4. Atrial flutter on the surface ECG. The underlying mechanism was a micro-reentry circuit at the septal side of the roofline.

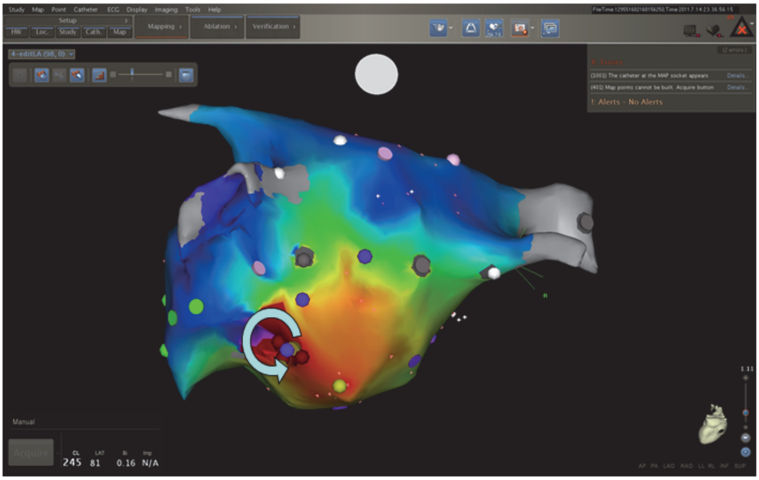


Figure 5. Carto activation map of a micro-reentry circuit as the basis of an atrial tachycardia with cycle length 270 ms, originating at the inferior LA (white arrow). PPI around the mitral annulus was > 30 ms. Focal radiofrequency application resulted in conversion to sinus rhythm.

Two patients had recurrence of persistent AF after hybrid AF ablation. In 1 patient, all PVs were still isolated. Complex fractionated atrial electrograms (CFAE) were found and subsequently ablated inside CS, at CS os and at the interatrial septum. The roofline was also re-ablated. Because of ongoing AF, ECV was needed to restore NSR. In the second patient with persistent AF, three out of four PVs showed reconnection (both left PVs and the right superior PV). They were successfully re-isolated with ostial RF applications. This resulted in conversion to a focal AT at the roof of the LA (between the roofline and mitral valve annulus) which was successfully ablated.

Two patients showed paroxysmal AF after hybrid AF ablation. The first patient was in NSR during EPS and showed reconnection of both right PVs. In this particular patient it was already noted during the hybrid procedure that it was not possible to guide the bipolar RF clamp completely around the right PVs. At the junction of the right superior PV with the roof of the LA (septal part of the roofline) we found low-amplitude fragmented signals (Figure 6). Application of cryo-energy at this spot, resulted in complete isolation of both right PVs. The second patient with recurrent paroxysmal AF, had AF at the start of EPS. All PVs were isolated. Ablation of CFAE at the interatrial septum resulted in conversion to a focal AT which was successfully ablated at the ostium of the CS. The mitral isthmus was also re-ablated.

One patient had recurrence of a typical AFL after hybrid procedure, which was successfully ablated at the CTI.

In this group of 9 patients, 5 (14%) out of 36 mapped PVs showed reconnection.

The long-term outcome after EPS and ablation is summarized in Table 6. The median follow-up was 27±11 months (range 9-43). There were 2 recurrences after EPS in this group of patients: 1 patient with persistent AF which was treated with rate control and 1 patient with AT which was treated with amiodarone.

Table 6. Outcomes of EPS and ablation in patients with recurrent arrhythmia after hybrid AF ablation procedure.

Patient	Duration of follow-up after CA (months)	Symptomatic recurrence	Monitoring (type and result)	AAD
1	30	No	7-day Holter, no recurrence	No
2	43	No	7-day Holter, no recurrence	No
3	35	No	7-day Holter, no recurrence	Flecainide
4	39	No	7-day Holter, no recurrence	Flecainide
5	10	Yes	7-day Holter, persistent AF	Betablocker, digitalis
6	27	No	7-day Holter, no recurrence	No
7	24	No	48h Holter, no recurrence	No
8	27	No	7-day Holter, no recurrence	No
9	9	Yes	7-day Holter, AT recurrence	Amiodarone

EPS = electrophysiological study, AF = atrial fibrillation, CA = catheter ablation, AT = atrial tachycardia, AAD = antiarrhythmic drug

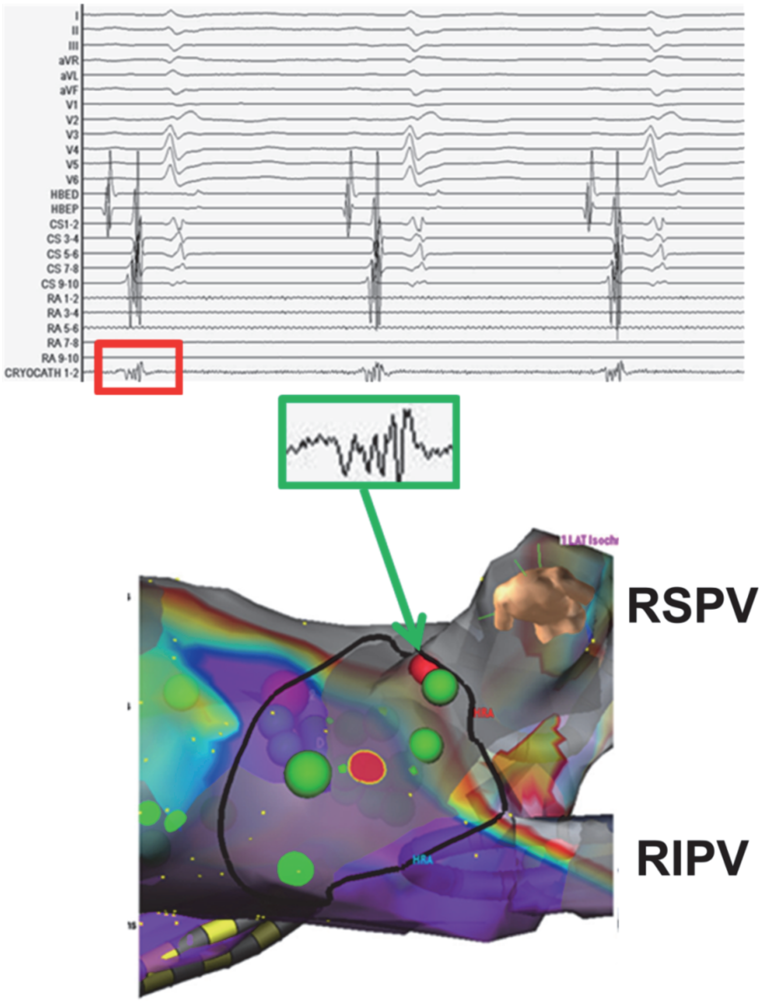


Figure 6. The upper part shows surface ECG (I to V6) and endocardial tracings (HB = His bundle, CS = coronary sinus, RA = right atrium (not connected), cryocath = cryo ablation catheter). The cryo ablation catheter is located at the junction of the upper part of the right superior PV with the LA roof and shows low amplitude, fragmented signals (small red box). This is the site of gap in the roof line. The EnSite map with the location of the low amplitude, fragmented signals at the gap in the roof line (green arrow and box).
RSPV = right superior PV, RIPV = right inferior PV

Medical therapy

The baseline characteristics, treatments, and outcomes for the 3 patients who were treated with medical therapy, are shown in Table 7. All 3 patients had recurrence of paroxysmal AF after hybrid ablation. Two patients were treated with amiodarone but, despite this medication, had still short AF episodes. One patient was treated with sotalol and experienced no arrhythmia anymore.

Table 7. Arrhythmia characteristics for patients with medical therapy for recurrent arrhythmia after hybrid AF ablation

Patient	AF type	AF duration (months)	Time from surgery to arrhythmia recurrence (days)	Previous CA	Recurrent arrhythmia type	AAD	Monitoring (type and result)
1	Pers	156	329	Yes	Parox AF	Amiodarone	ECG, Parox AF
2	Parox	24	148	No	Parox AF	Sotalol	ECG, NSR
3	Pers	12	70	No	Parox AF	Amiodarone	PM, Parox AF

AF = atrial fibrillation, Pers = persistent, Parox = paroxysmal, CA = catheter ablation, AAD = antiarrhythmic drug, ECG = electrocardiogram, NSR = normal sinus rhythm, PM = pacemaker

Complications

No deaths or conversion to cardiopulmonary bypass were encountered during hybrid AF ablation. No patient demonstrated paralysis of the phrenic nerve. One patient had a pleural effusion drained 3 weeks after surgery. One patient had a mini thoracotomy because of hemothorax but no active bleeding was found. One patient stayed hospitalized for 13 days because of difficulty controlling chest pain at the insertion sites of the working ports, without signs of infection. One patient developed adult respiratory stress syndrome and was successfully treated with steroids and antibiotics.

Discussion

Main findings

This is the first report on long-term follow-up of hybrid thoracoscopic surgical and transvenous catheter ablation for AF. Fifty-six patients were followed during at least two years. Twelve patients had an arrhythmia recurrence which was treated with EPS and ablation or AADs. According to accepted definitions, our overall 2-year freedom from arrhythmia without AADs was 85%. At 4 year follow-up, this was the case in 80% of patients.

Long-term follow-up

Until recently, studies reporting outcomes of AF ablation had mostly limited follow-up to 1 to 2 years after the first ablation procedure.[1, 6, 7] Weerasooriya et al. reported 63% freedom from recurrent AF by 5 years of follow-up, with repeat interventions in 51% of patients.[8] In this study, 63% of patients had paroxysmal AF. Results from the Hamburg group were comparable: 47% of paroxysmal AF patients remained in NSR after the initial procedure during a median follow-up period of 4.8 years.[9] The same group published recently their long-term follow-up after ablation of long-standing persistent AF: during a 5-year follow-up, single- and multiple ablation procedure success was 20% and 45%, respectively.[10] Surgical AF ablation, on the other hand, seems to result in improved long-term results. Prasad et al. reported up to 97% success at a median follow-up of 5,4±2,9 years after Cox-maze III procedure. However, it should be stated that one of the major criticism on these published results is that success rate was based mostly on telephone interviews and ECG strips, and very seldom on 24h or longer Holter monitoring.[11] Another draw-back of the Cox-maze III procedure is its invasiveness and surgical complexity. In our series of patients with long-term follow-up after hybrid ablation for AF, we demonstrated an overall success rate (freedom of any AF/AFL/AT episode longer than 30 seconds off AAD) of 85% at 2 years and 80% at 4 years. These promising results reflect the complementarity of both techniques. Indeed, in 16% of the patients endocardial touch-up was necessary to complete the box lesion. The unique combination of epicardial surgical ablation lesions with endocardial mapping and touch-up abilities, seems to result in a more longlasting aspect of the lesion set in a given patient.

Recurrent arrhythmias

The incidence of recurrent ATs after endocardial ablation of persistent AF goes up to 40%.[12] Rostock et al. analyzed a total number of 133 ATs that occurred after stepwise ablation in 61 patients with persistent AF.[13] The redo procedure was performed at a mean of 7.7±4.4 months after initial de novo ablation. The arrhythmia mechanism was based on reentry in 72% and 28% were focal ATs. Roof and perimitral flutter (43% and 34%, respectively) were the most common reentrant circuits. Focal ATs mainly originated from pulmonary veins (41%) and coronary sinus (23%). They also found that 74% of patients had conduction recovery of at least 1 pulmonary vein. Almost all these ATs (93%) could be successfully ablated. Kron et al. reported recurrent AT in 40% of patients after minimally invasive thoracoscopic surgical PV isolation and GP ablation during a minimal follow-up of 12 months. In patients that underwent EPS, the most common arrhythmias documented were AF and AFL. In patients with recurrent AF, PV reconnection was the predominant finding: of 44 PVs examined, 22 (50%) reconnected. Four AFLs were seen: 2 were CTI dependent, 1 was located at the posterior right atrium and the mechanism of 1 left AFL could not be determined. Only 1 patient had a focal AT at the left septum. In our series of 56 patients with hybrid AF ablation, we report an arrhythmia recurrence rate of 21% after a follow-up of up to 4 years. The most frequent occurring recurrent arrhythmias were left AFL and AF. Left AFL occurred in 4 patients and in 2 of them the reentry circuit was the result of an incomplete linear lesion. In the remaining two patients with left AFL, the circuit appeared not to be related to the lesion set deployed during hybrid AF ablation. In the 4 patients with recurrent AF, 2 showed reconnection of PVs: 1 patient had reconnection of both left PVs and the right superior PV, and 1 patient had reconnection of both right PVs. In the latter patient, the bipolar RF clamp used during hybrid AF ablation to isolate the right PVs 'en bloc', appeared to be too short. It was not possible to place the upper part of the antrum (junction of the right superior PV with the LA roof) between the 2 jaws of the clamp. RF application with the clamp resulted in acute isolation of both right PVs but subsequent recovery of conduction at that spot, led to reconnection. In order to avoid this phenomenon in the future, we changed our approach and always perform an endocardial touch-up whenever the bipolar clamp does not completely encompass the antrum of ipsilateral PVs (Figure 7).

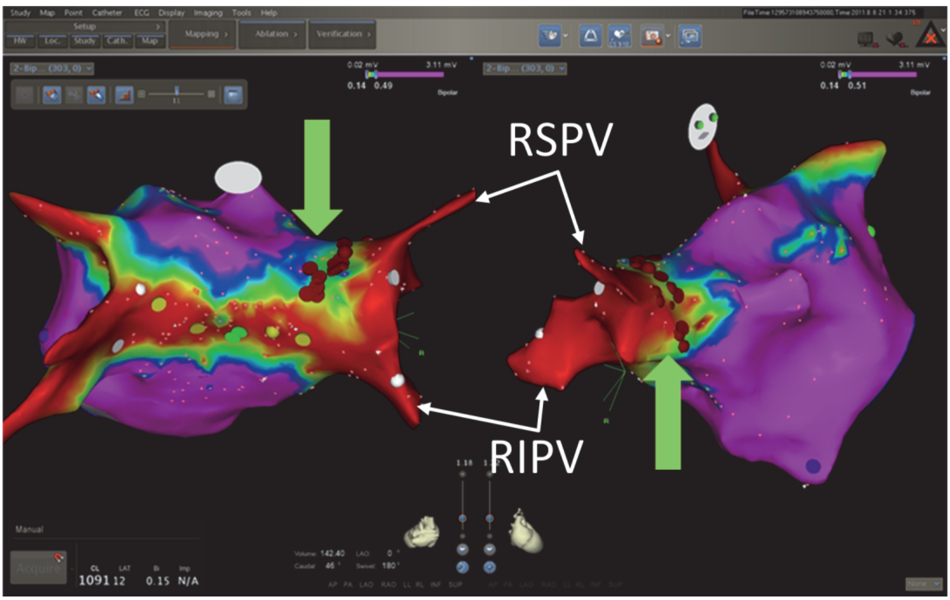


Figure 7. Intra-operative endocardial touch-up (red dots, green arrow) at the junction of the right superior PV with the LA roof in a patient where the bipolar RF clamp was too short. The box lesion is complete and clearly visible on the Carto voltage map (red area).
RSPV = right superior pulmonary vein, RIPV = right inferior pulmonary vein.

Pulmonary vein reconnection after initial PV isolation, remains the most important reason for AF recurrence.[14] It is present in more than 80% of patients who undergo a repeat procedure.[4, 15, 16] The use of a bipolar RF clamp with bilateral clamping of the PVs as in our study, seems to result in permanent transmurality in almost all of our cases.[17, 18] It remains unclear however, why Kron et al., while using the same device to perform PV isolation, reported 50% PV reconnection. In our series this was the case in only 14% of the tested PVs. A possible explanation for this intriguing finding could be the difference in the number of RF applications. Kron et al. performed 1 to 5 (mean 3) additional bonus lesions after the first RF application. In our series we performed at least 6 RF applications per PV antrum in order to avoid incomplete lesions. The reason to perform this relatively high minimum number of applications in our series, is the fact that the length of each application is dictated by the bipolar RF generator itself. The generator automatically terminates RF energy (maximum 28 W) after a prespecified impedance change that is believed to indicate transmural injury. However, the presence of epicardial fat and thicker atrial tissue may influence these impedance changes and hence lead to the wrong conclusion that a specific impedance change is indicative of complete transmurality.

This study seems to indicate that bipolar, bilateral RF clamp ablation is extremely effective in producing definitive PV isolation. This may warrant a primary hybrid ablation procedure in patients in whom one single procedure is preferred above the foresight of a series of repeated percutaneous CA procedures.

Sinus rhythm as endpoint of AF ablation

The endpoint of persistent AF ablation is still an area of debate.[1, 19, 20] Ammar et al. published very recently their experience in a series of 191 consecutive patients undergoing de novo catheter ablation for symptomatic persistent and long-standing persistent AF.[21] Patients were classified into 3 groups according to the rhythm at the end of procedure: patients with termination of AF into NSR , patients with AT undergoing ECV, or patients with AF undergoing ECV. At 12 months, termination into NSR was associated with a significantly lower risk of arrhythmia recurrence. This finding was also true in our series: the group of patients with recurrent arrhythmia after hybrid AF ablation, was characterized by a significantly higher need for ECV at the end of the procedure. The 4 patients that needed ECV at the end of hybrid AF ablation procedure, developed arrhythmia recurrence during follow-up.

Study limitations

The small number of patients in this single-center retrospective study prevents definitive conclusions. Although only one patient had isolated PVs after previous CA, we cannot exclude that previous CA favorably influenced the results. In the present series, the overall clinical success may have not recognized some episodes of asymptomatic arrhythmia by the relatively short periods of ambulatory monitoring performed. The safety of this procedure may be a concern because of the extent of ablation and the full heparinization during the procedure. An ablation strategy based on noninducibility could lead to overtreatment of some patients. The success rate in patients with persistent AF was not significantly lower than in patients with paroxysmal AF. This may be explained by the relatively low number of included patients but it may also reflect the effectiveness of this approach. Not all patients with recurrent arrhythmia after hybrid AF ablation procedure, underwent EPS.

Conclusions

A combined hybrid thoracoscopic surgical and transvenous catheter ablation procedure for AF, has a two-year success of 82% for patients with paroxysmal AF and 88% for patients with non-paroxysmal AF. At 4 year follow-up, success rates were 75% for patients with paroxysmal AF and 87% for patients with non-paroxysmal AF. Bipolar, bilateral RF clamp ablation seems extremely effective in producing definitive PV isolation and may appear useful in patients in whom a one time procedure is preferred above the foresight of repeated percutaneous CA procedures. Recurrent supraventricular arrhythmias can be treated with CA or AADs.

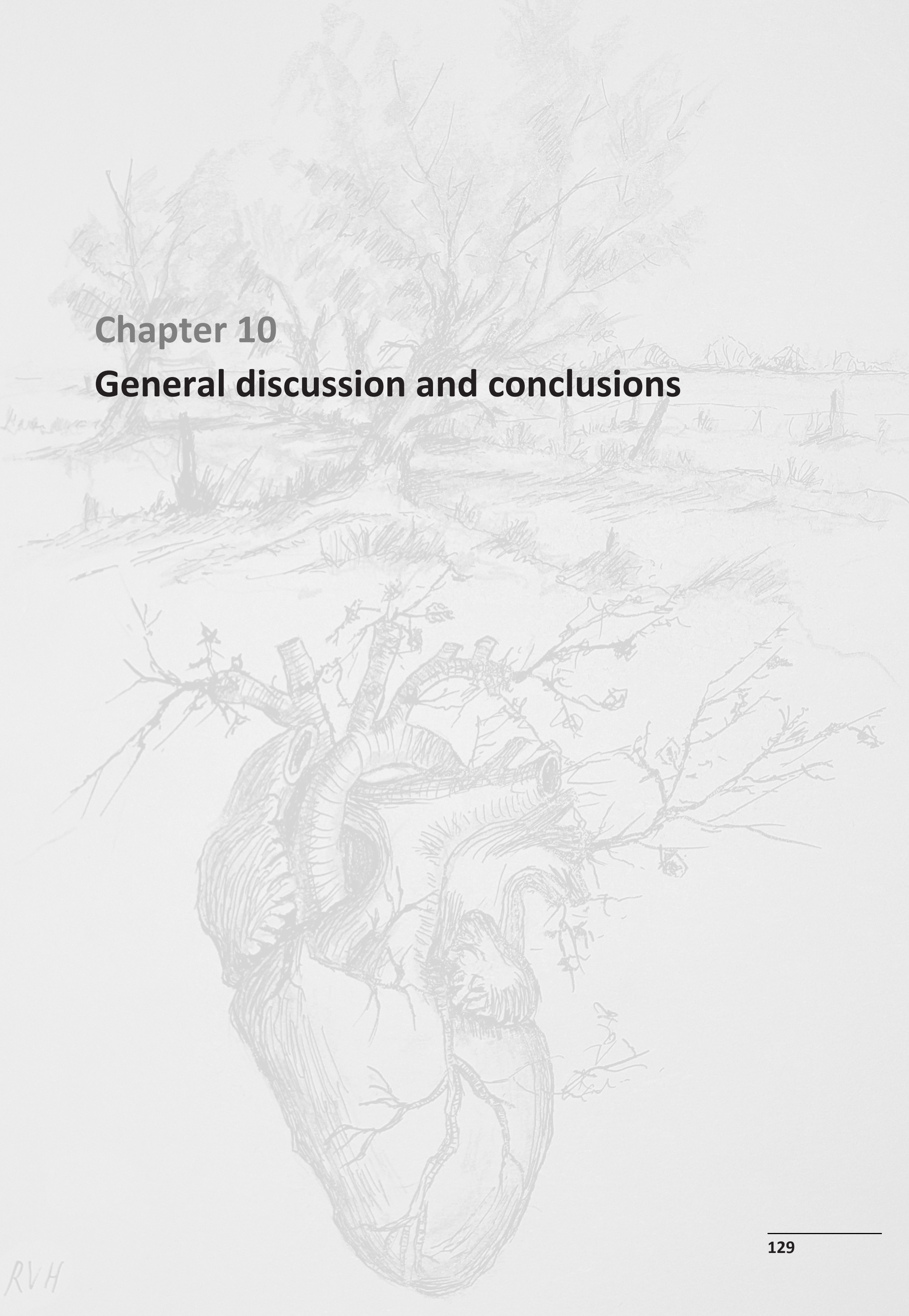
References

1. Calkins H, Kuck KH, Cappato R, Brugada J, Camm AJ, Chen SA, Crijns HJ, Damiano RJ, Jr., Davies DW, DiMarco J, Edgerton J, Ellenbogen K, Ezekowitz MD, Haines DE, Haissaguerre M, Hindricks G, Iesaka Y, Jackman W, Jalife J, Jais P, Kalman J, Keane D, Kim YH, Kirchhof P, Klein G, Kottkamp H, Kumagai K, Lindsay BD, Mansour M, Marchlinski FE, McCarthy PM, Mont JL, Morady F, Nademanee K, Nakagawa H, Natale A, Nattel S, Packer DL, Pappone C, Prystowsky E, Raviele A, Reddy V, Ruskin JN, Shemin RJ, Tsao HM, Wilber D. 2012 hrs/ehra/ecas expert consensus statement on catheter and surgical ablation of atrial fibrillation: Recommendations for patient selection, procedural techniques, patient management and follow-up, definitions, endpoints, and research trial design. *Europace : European pacing, arrhythmias, and cardiac electrophysiology : journal of the working groups on cardiac pacing, arrhythmias, and cardiac cellular electrophysiology of the European Society of Cardiology*. 2012;14:528-606
2. Nault I, Miyazaki S, Forclaz A, Wright M, Jadidi A, Jais P, Hocini M, Haissaguerre M. Drugs vs. Ablation for the treatment of atrial fibrillation: The evidence supporting catheter ablation. *European heart journal*. 2010;31:1046-1054
3. Dewire J, Calkins H. Update on atrial fibrillation catheter ablation technologies and techniques. *Nature reviews. Cardiology*. 2013;10:599-612
4. Medi C, Sparks PB, Morton JB, Kistler PM, Halloran K, Rosso R, Vohra JK, Kumar S, Kalman JM. Pulmonary vein antral isolation for paroxysmal atrial fibrillation: Results from long-term follow-up. *Journal of cardiovascular electrophysiology*. 2011;22:137-141
5. Pison L, La Meir M, van Opstal J, Blaauw Y, Maessen J, Crijns HJ. Hybrid thoracoscopic surgical and transvenous catheter ablation of atrial fibrillation. *Journal of the American College of Cardiology*. 2012;60:54-61
6. Bunch TJ, Day JD. Achieving favorable very long-term outcomes after catheter ablation for atrial fibrillation: An exciting adventure or delusional quest? *Journal of cardiovascular electrophysiology*. 2011;22:1215-1216
7. European Heart Rhythm A, European Association for Cardio-Thoracic S, Camm AJ, Kirchhof P, Lip GY, Schotten U, Savelieva I, Ernst S, Van Gelder IC, Al-Attar N, Hindricks G, Prendergast B, Heidbuchel H, Alfieri O, Angelini A, Atar D, Colonna P, De Caterina R, De Sutter J, Goette A, Gorenek B, Heldal M, Hohloser SH, Kolh P, Le Heuzey JY, Ponikowski P, Rutten FH. Guidelines for the management of atrial fibrillation: The task force for the management of atrial fibrillation of the european society of cardiology (esc). *European heart journal*. 2010;31:2369-2429
8. Weerasooriya R, Khairy P, Litalien J, Macle L, Hocini M, Sacher F, Lellouche N, Knecht S, Wright M, Nault I, Miyazaki S, Scavee C, Clementy J, Haissaguerre M, Jais P. Catheter ablation for atrial fibrillation: Are results maintained at 5 years of follow-up? *Journal of the American College of Cardiology*. 2011;57:160-166
9. Ouyang F, Tilz R, Chun J, Schmidt B, Wissner E, Zerm T, Neven K, Kokturk B, Konstantinidou M, Metzner A, Fuernkranz A, Kuck KH. Long-term results of catheter ablation in paroxysmal atrial fibrillation: Lessons from a 5-year follow-up. *Circulation*. 2010;122:2368-2377
10. Tilz RR, Rillig A, Thum AM, Arya A, Wohlmuth P, Metzner A, Mathew S, Yoshiga Y, Wissner E, Kuck KH, Ouyang F. Catheter ablation of long-standing persistent atrial fibrillation: 5-year outcomes of the hamburg sequential ablation strategy. *Journal of the American College of Cardiology*. 2012;60:1921-1929
11. Ad N, Henry L, Hunt S, Barnett S, Stone L. The cox-maze iii procedure success rate: Comparison by electrocardiogram, 24-hour holter monitoring and long-term monitoring. *The Annals of thoracic surgery*. 2009;88:101-105
12. Brooks AG, Stiles MK, Laborderie J, Lau DH, Kuklik P, Shipp NJ, Hsu LF, Sanders P. Outcomes of long-standing persistent atrial fibrillation ablation: A systematic review. *Heart rhythm : the official journal of the Heart Rhythm Society*. 2010;7:835-846
13. Rostock T, Drewitz I, Steven D, Hoffmann BA, Salukhe TV, Bock K, Servatius H, Aydin MA, Meinertz T, Willems S. Characterization, mapping, and catheter ablation of recurrent atrial tachycardias after stepwise ablation of long-lasting persistent atrial fibrillation. *Circulation. Arrhythmia and electrophysiology*. 2010;3:160-169

14. Calkins H, Kuck KH, Cappato R, Brugada J, Camm AJ, Chen SA, Crijns HJ, Damiano RJ, Jr., Davies DW, DiMarco J, Edgerton J, Ellenbogen K, Ezekowitz MD, Haines DE, Haissaguerre M, Hindricks G, Iesaka Y, Jackman W, Jalife J, Jais P, Kalman J, Keane D, Kim YH, Kirchhof P, Klein G, Kottkamp H, Kumagai K, Lindsay BD, Mansour M, Marchlinski FE, McCarthy PM, Mont JL, Morady F, Nademanee K, Nakagawa H, Natale A, Nattel S, Packer DL, Pappone C, Prystowsky E, Raviele A, Reddy V, Ruskin JN, Shemin RJ, Tsao HM, Wilber D, Heart Rhythm Society Task Force on C, Surgical Ablation of Atrial F. 2012 hrs/ehra/ecas expert consensus statement on catheter and surgical ablation of atrial fibrillation: Recommendations for patient selection, procedural techniques, patient management and follow-up, definitions, endpoints, and research trial design: A report of the heart rhythm society (hrs) task force on catheter and surgical ablation of atrial fibrillation. Developed in partnership with the european heart rhythm association (ehra), a registered branch of the european society of cardiology (esc) and the european cardiac arrhythmia society (ecas); and in collaboration with the american college of cardiology (acc), american heart association (aha), the asia pacific heart rhythm society (aphrs), and the society of thoracic surgeons (sts). Endorsed by the governing bodies of the american college of cardiology foundation, the american heart association, the european cardiac arrhythmia society, the european heart rhythm association, the society of thoracic surgeons, the asia pacific heart rhythm society, and the heart rhythm society. *Heart rhythm : the official journal of the Heart Rhythm Society*. 2012;9:632-696 e621
15. Ouyang F, Bansch D, Ernst S, Schaumann A, Hachiya H, Chen M, Chun J, Falk P, Khanedani A, Antz M, Kuck KH. Complete isolation of left atrium surrounding the pulmonary veins: New insights from the double-lasso technique in paroxysmal atrial fibrillation. *Circulation*. 2004;110:2090-2096
16. Verma A, Kilicaslan F, Pisano E, Marrouche NF, Fanelli R, Brachmann J, Geunther J, Potenza D, Martin DO, Cummings J, Burkhardt JD, Saliba W, Schweikert RA, Natale A. Response of atrial fibrillation to pulmonary vein antrum isolation is directly related to resumption and delay of pulmonary vein conduction. *Circulation*. 2005;112:627-635
17. Prasad SM, Maniar HS, Diodato MD, Schuessler RB, Damiano RJ, Jr. Physiological consequences of bipolar radiofrequency energy on the atria and pulmonary veins: A chronic animal study. *The Annals of thoracic surgery*. 2003;76:836-841; discussion 841-832
18. Gaynor SL, Ishii Y, Diodato MD, Prasad SM, Barnett KM, Damiano NR, Byrd GD, Wickline SA, Schuessler RB, Damiano RJ, Jr. Successful performance of cox-maze procedure on beating heart using bipolar radiofrequency ablation: A feasibility study in animals. *The Annals of thoracic surgery*. 2004;78:1671-1677
19. O'Neill MD, Wright M, Knecht S, Jais P, Hocini M, Takahashi Y, Jonsson A, Sacher F, Matsuo S, Lim KT, Arantes L, Derval N, Lellouche N, Nault I, Bordachar P, Clementy J, Haissaguerre M. Long-term follow-up of persistent atrial fibrillation ablation using termination as a procedural endpoint. *European heart journal*. 2009;30:1105-1112
20. Estner HL, Hessling G, Ndrepepa G, Luik A, Schmitt C, Konietzko A, Ucer E, Wu J, Kolb C, Pflaumer A, Zrenner B, Deisenhofer I. Acute effects and long-term outcome of pulmonary vein isolation in combination with electrogram-guided substrate ablation for persistent atrial fibrillation. *The American journal of cardiology*. 2008;101:332-337
21. Ammar S, Hessling G, Reents T, Paulik M, Fichtner S, Schon P, Dillier R, Kathan S, Jilek C, Kolb C, Haller B, Deisenhofer I. Importance of sinus rhythm as endpoint of persistent atrial fibrillation ablation. *Journal of cardiovascular electrophysiology*. 2013;24:388-395

Chapter 10

General discussion and conclusions



A. General discussion

1. Atrial fibrillation pathophysiology: implications for invasive management

Based on presentation and duration, atrial fibrillation (AF) can be categorized as first diagnosed, paroxysmal, persistent, long-standing persistent and permanent.[1] Paroxysmal AF is self-terminating, usually within 48 h. When AF lasts longer than 7 days or when cardioversion is required, it is persistent. Long-standing persistent AF is defined as continuous AF for at least 1 year. AF becomes permanent when its presence is accepted.

The characteristic irregular atrial discharge during AF, may be caused by a rapidly and regularly firing driver.[2] The underlying mechanism of this driver may be local ectopic firing or a single localized reentry circuit. Multiple functional reentry circuits varying in time and space may also maintain AF in the absence of a driver.

Paroxysmal AF is generally caused by rapid focal activity or local reentry in the cardiac muscle sleeve which extends from the left atrium (LA) around one or more pulmonary veins (PV).[3] Jahangir et al. analyzed the rate of progression from lone paroxysmal AF to permanent AF over almost 30 years.[4] They found that 41% of the paroxysmal AF patients evolve to permanent AF. The evolution towards more persistent AF episodes, is associated with atrial remodeling which is caused by progression of coexisting heart disease or the arrhythmia itself.[5, 6] Atrial remodeling may manifest itself in 3 ways: electrical remodeling, structural remodeling and neural remodeling.

Very rapid atrial tachyarrhythmias like AF, result in increased cellular Ca^{2+} loading. In order to reduce Ca^{2+} entry into the cell, Ca^{2+} current is inactivated and I_{CaL} downregulated.[2, 7-9] To further decrease Ca^{2+} loading, action potential duration (APD) becomes shorter by inward rectifier K^+ current (I_{K1} and I_{KAChCh}) enhancement. This APD reduction results in stabilization of atrial reentry circuits and, as a consequence of this phenomenon, increased AF vulnerability and sustainability. Electrical remodeling leads to drug resistance of non-paroxysmal AF and progression from paroxysmal to more persistent forms.

Fibrosis is the cornerstone of structural remodeling. By separating muscle bundles and replacing cardiomyocytes, fibrosis results in loss of electrical continuity and conduction slowing.[10, 11] Electrical coupling of fibroblasts with cardiomyocytes, improves reentry and ectopic activity.[12] AF itself may support and induce structural remodeling, hence promoting its evolution to more persistent forms.[13]

Autonomic neural remodeling is partially based on enhanced I_{KACh} current due to vagal discharge.[14] This results in APD shortening and stabilization of reentry circuits. β-Adrenoreceptor activation promotes diastolic Ca^{2+} leak and delayed after depolarozation-related focal ectopic activity.[15] Atrial sympathetic hyperinnervation has been shown in patients with non-paroxysmal AF.[16] This form of remodeling results in AF persistence and recurrence.

Whereas paroxysmal AF is predominantly driven by focal activity or local reentry from one or more PVs, as the arrhythmia evolves towards more persistent forms promoted by the several types of atrial remodeling, AF-maintaining mechanisms move towards the atria and are increasingly based on reentry substrates.[5, 6, 17] These reentry substrates seem to be functional initially and they become structural as time progresses.

These pathophysiological concepts are the foundations on which current ablation strategies are build. In the vast majority of patients with paroxysmal AF, the ablation procedure should target the PVs with complete electrical isolation as an endpoint.[3, 18-20] In patients with non-paroxysmal AF, however, PV isolation alone seems to be insufficient to prevent the arrhythmia.[19, 21-23] The pathophysiological processes in the more-sustained forms of this arrhythmia, seem to justify an ablation strategy that, besides the PVs, also addresses the arrhythmogenic substrate in the atria.

2. Hybrid therapy for atrial fibrillation: where the knife meets the catheter

According to the most recent Heart Rhythm Society(HRS)/European Heart Rhythm Society(EHRA)/European Cardiac Arrhythmia Society (ECAS) consensus statement, both the endocardial and stand alone surgical AF ablation approach can be considered in patients with symptomatic AF refractory or intolerant to at least one Vaughan-Williams class 1 or 3 AAD but the current evidence supporting surgical ablation is mainly based on expert consensus and clinical experience. The indication to perform an endocardial ablation in this kind of patients, however, is driven by results from randomized clinical trials and/or meta-analyses.[19]

As the strengths of both techniques seem to overcome their mutual weaknesses, several groups tried to combine both approaches in the hope to further improve results of AF ablation.

In this chapter we will first briefly review the current status of endocardial and surgical ablation techniques in order to better understand the rationale for a hybrid or convergent concept. The second part will focus on the several aspects of the hybrid AF ablation with the emphasis on techniques, follow-up and outcomes.

a. Endocardial AF ablation

The cornerstone of endocardial AF ablation is an ablation strategy that targets the PV and/or PV antrum whereby electrical isolation of the PV should be the goal.[19] The one-year success rate of this approach is greater than 80% in patients with paroxysmal AF.[24] Nowadays, unipolar radiofrequency (RF) is the most frequently used energy source to perform PV isolation. Cryoablation and laser are two alternatives.[25, 26] Whatever energy source used, the most frequent reason for AF recurrence after PV isolation remains PV reconduction.[27] Long-term results of catheter ablation for paroxysmal AF are somewhat disappointing: in a recently published prospective study, sinus rhythm was maintained in only 46% of patients after the initial procedure without AAD during a median follow-up period of 5 years.[28] As AF progresses from paroxysmal to persistent and longstanding persistent AF, the atrial substrate itself plays an increasingly important role in the maintenance of the arrhythmia.[29] This may explain why PV isolation alone results in success rates of less than 25% in patients with persistent AF.[30] To improve these results, one needs to modify the atrial substrate by creating linear lesions and/or ablating complex fractionated atrial electrograms (CFAE). Ablation procedures combining PV isolation with linear lesions and/or CFAE ablation in patients with (longstanding) persistent AF, seem to result in better outcomes than PV isolation alone but there is an important variation in success rates ranging from 11% to 75% and the incidence of iatrogenic atrial tachycardias after these procedures is substantial (up to 40%).[31, 32] The creation of linear lesions was inspired by the surgical Cox-maze procedure for AF.[33] These linear lesions are thought to prevent sustained multiple re-entry circuits by compartmentalization of the atria. The two most frequently deployed endocardial linear lesions, are the roofline connecting both superior PVs and the mitral isthmus line going from the left inferior PV to the mitral annulus. However, performing these linear lesions can sometimes be very challenging and incomplete lines may act as a substrate for macro-re-entrant circuits.[34] In 2004, Nademanee et al reported a one year success rate of 87% in patients with persistent AF (4% with AAD) and 78% in patients with longstanding persistent AF (11% with AAD) after CFAE (defined as fractionated electrograms with 2 or more deflections and a mean cycle length shorter than 120 ms) ablation only.[35] However, those results could not be reproduced by other groups and the electrophysiological mechanisms underlying CFAEs are still a source of debate.[36-38] Sites demonstrating high-dominant frequency seem to be as well interesting ablation sites. In an animal model, these sites correspond to functional reentry and are called rotors.[39] Recently, localized rotors have been visualized in human AF by computational mapping and ablation of these rotors results in acute termination of AF or substantial organization of the arrhythmia.[40, 41] This discovery holds the potential for an important step towards a tailored substrate ablation approach, especially in patients with persistent AF.

b. Surgical AF ablation

The gold standard for the surgical treatment of AF is the Cox-maze III procedure, also known as the "cut-and-sew" maze. This operation involves the creation of numerous incisions in both atria that would direct the sinus impulse propagation through the atria while interrupting macro-re-entrant circuits.[42] This procedure results in impressive long term success rates with 92% of patients free from symptomatic AF and 80% off AAD.[43] Postoperative care was standardized and included regular follow-up appointments with ECG monitoring. Importantly, the use of holter monitors, pacemaker interrogation, implantable monitoring devices, were not routine and therefore the results most likely overestimate the success. Another advantage of the surgical approach, is the possibility of removing the left atrial appendage (LAA) which may help to decrease the risk for stroke, especially in patients with a contraindication for warfarin.[44] According to the

HRS/EHRA/ECAS expert consensus statement on catheter and surgical ablation of AF, stand-alone AF surgery should be considered for symptomatic AF patients who are refractory or intolerant to at least one Class 1 or 3 AAD, prefer a surgical approach or have failed one or more attempts at catheter ablation.[19] Nevertheless, the Cox-maze III procedure did not gain widespread implementation due to its complexity and technical challenge. As an alternative to the surgical incisions of the cut-and-sew maze and in an effort to simplify the procedure, several groups replaced these incisions with linear lines of ablation. In 2004, Damiano et al. introduced the Cox-maze IV procedure during which bipolar RF devices were used to isolate the PVs and create linear lesions.[45] This procedure can be performed through a small thoracotomy but it still requires cardiopulmonary bypass. There appears to be no difference between the Cox-maze III and IV procedure in terms of the rate of freedom from AF at 3, 6, and 12 months.[46] The last decade has been marked by a quest for new surgical ablation devices using unipolar and bipolar RF, microwave, laser, cryoablation or high-frequency ultrasound, that would enable the cardiac surgeon to perform a curative lesion epicardially on the beating heart without the need for cardiopulmonary bypass.[47] Unfortunately, none of the currently existing energy sources is able to guarantee reliable, transmural lesions in each and every patient. Another shortcoming of the epicardial surgical approach, is the inability to map and selectively ablate any re-entrant or focal tachycardia occurring during surgical AF ablation. Current techniques for the minimally invasive surgical treatment of stand-alone AF, result in success rates (defined as freedom from any AF episode longer than 30 seconds off AAD) at 12 months from 65% to 92% in paroxysmal AF and from 67% to 80% in persistent AF.[47]

c. The hybrid AF ablation procedure: the best of two worlds

Given the current knowledge about etiology and pathophysiology of AF, an optimal ablation procedure for this arrhythmia would [1] isolate the PVs permanently, [2] define the specific properties of the underlying atrial electrical substrate in order to customize the subsequent ablation strategy, [3] always create completely transmural linear lesions when indicaded, and [4] be minimally invasive. To date, neither the endocardial approach nor the surgical ablation procedure on its own is able to meet all these criteria. However, both techniques seem to be complementary as, performed in combination (hence the nomenclature “hybrid” or “convergent” procedure), they bear the potential to overcome their respective shortcomings. The epicardial surgical approach seems to result in superior transmurality of the lesions, resulting in longlasting PV isolation and permanent conduction block, especially when using bipolar RF.[48, 49] The endocardial AF ablation procedure on the other hand, using multipolar catheters and three-dimensional electroanatomical mapping systems, is the most efficacious setting to guide substrate modification and ablation of atrial tachycardias known to occur during the stepwise ablation of persistent AF.[50] Another important advantage of the hybrid approach is the possibility of performing endocardial touch-up in case of an epicardial lesion that is not completely transmural.

There appears to be a wide variation in the possible combinations of epicardial surgical and transvenous endocardial techniques, lesion sets, and follow-up used for hybrid or convergent AF ablation procedures.[51, 52]

This multidisciplinary approach makes it possible to create and evaluate an extensive biatrial lesion set, without sternotomy or cardiopulmonary bypass. To date, the number of patients who underwent a hybrid AF ablation remains small but, especially in patients with persistent and longstanding persistent AF, one-year success rates off AAD are promising. However, different hybrid or convergent ablation strategies, various energy sources and divergent definitions of success are being used which makes it quite difficult to compare outcomes. It is therefore not clear which lesions or lesion sets are needed and what is the best endpoint for this kind of procedures. The only lesion they all have in common is PV isolation. Isolation of the posterior wall of the LA is also a preferred target as ectopy initiating AF frequently arises in this part of the LA.[53] The added value of GP ablation is still an area of debate. In an animal model, Damiano et al. demonstrated functional reinnervation within a period of 4 weeks.[54] The concern has been raised that if this reinnervation is non-uniform, this could create a new substrate for AF that was not originally present in a given patient. Another advantage of the hybrid approach, is the possibility to exclude the LAA as this is the site of most of the clot formation that eventually leads to thromboembolic events in patients with non-valvular AF.[55] In addition, there may be a small number of patients with recurrent AF owing to a trigger nestled in the LAA, which could be eliminated with exclusion of this appendage.[56] Combining the epicardial surgical and the endocardial approach in one single procedure makes it possible to perform an endocardial touch-up whenever epicardial lesions are not completely transmural. Other advantages are [1] the anatomic guiding for those touch-up lesions by the surgeon showing the cardiologist where the epicardial lesions are exactly located and [2] the immediate add on endocardial lesion and the already deployed surgical lesions add up to form a firm transmural lesion. However, organizing this kind of procedures requires robust logistical capacities as both the cardiac surgeon and electrophysiologist need to be in the same room at the same time. Another important concern is that performing an endocardial ablation immediately after epicardial ablation rather than staging endocardial ablation at a later date, may limit endocardial mapping due to edema or transient injury caused by epicardial ablation. However, considering the long term results of the combined approach this probably is not a true problem. Whether to perform a hybrid AF ablation in a given patient rather than a standard endocardial procedure, remains a difficult question as long as we don’t have results of prospective randomized trials at our disposal. Current data suggest to reserve this kind of procedures for patients with persistent or longstanding persistent AF with a dilated LA or after a failed endocardial approach. The significant complication rate in some series is likely the effect of a learning curve as this kind of procedures requires a specific technical expertise concerning the epicardial surgical aspect. In order to further improve widespread acceptance and implementation of these hybrid techniques, major complications should be restricted to a minimum.

B. Conclusions

Our understanding of the precise pathophysiological mechanisms underlying AF is still incomplete. This is one of the major reasons why, especially in non-paroxysmal AF, the optimal ablation approach remains the subject of intense debate and clinician choice, both for electrophysiologists and cardiac surgeons. Endocardial AF ablation techniques enable one to characterize the underlying substrate in order to tailor the ablation procedure but these ablation lesions are not always transmural nor long lasting. Surgical AF ablation techniques, on the other hand, create more reliable linear lesions but the lesion set is based on empirical assumptions rather than specific patient characteristics. Performed in combination, both approaches seem to be complementary as they overcome their mutual shortcomings. This setting makes it also possible to endocardially touch-up epicardial lesions that are not completely transmural or specific sites that are not accessible for the surgeon.

In this thesis, we demonstrated that the hybrid or convergent AF ablation procedure, resulting from the integration of endocardial transcatheter and epicardial off-pump surgical techniques, is safe and feasible. Medium and long-term results are encouraging, especially in currently challenging settings such as non-paroxysmal AF and failed endocardial catheter ablation procedures. As such, the hybrid approach has the potential to become an important tool in the armamentarium of cardiac surgeons and electrophysiologists that are dedicated to the invasive treatment of this arrhythmia.

Nevertheless, it remains of great importance to focus on the limitations of our findings. First of all, performing this kind of hybrid procedures requires efficient logistics as cardiac surgeon and electrophysiologist must both have to be in the same hospital at the same time. Secondly, one could prefer performing these procedures in a staged fashion (the epicardial surgical ablation followed by the endocardial ablation part on a separate day) rather than a single procedure. Surgeons may feel uncomfortable performing epicardial ablation in a patient that is fully heparanized. The third point, is that we opted for an ablation strategy based on PVI followed by a stepwise approach guided by noninducibility and concomitant patient diseases. This could have led to overtreatment in some patients. Finally, the limited number of patients in this single-center experience, prevents us to formulate definitive conclusions.

Where do we go from here? Several important challenges are to be met. We are in desperate need of a comprehensive pathophysiological model for AF. Such a model could allow ablationists to develop truly customized ablation strategies based on atrial electrophysiology rather than empiric lesions. It remains unclear why a specific lesion set is effective in some patients but not in others. A better understanding of the underlying arrhythmogenic mechanism, holds substantial promise for improving outcomes of AF ablation. The hybrid setting makes it possible to perform extensive mapping of the endocardium and epicardium simultaneously. Although generating encouraging results, the hybrid approach for AF needs to be compared with current endocardial ablation strategies in a prospective and randomized fashion. This will be the subject of the Combined Endoscopic Epicardial and Percutaneous Endocardial Ablation versus Repeated Catheter Ablation in Persistent and Longstanding Persistent Atrial Fibrillation trial (ELECTRA trial). The hybrid procedure requires a bilateral thoracoscopic approach to perform the epicardial ablation. Further improvement and miniaturization of the surgical equipment may allow a subxiphoidal approach. Future research should explore alternative energy sources used for the creation of epicardial lesions, in order to reduce the need for endocardial touch-ups.

References

1. European Heart Rhythm A, European Association for Cardio-Thoracic S, Camm AJ, Kirchhof P, Lip GY, Schotten U, Savelieva I, Ernst S, Van Gelder IC, Al-Attar N, Hindricks G, Prendergast B, Heidbuchel H, Alfieri O, Angelini A, Atar D, Colonna P, De Caterina R, De Sutter J, Goette A, Gorenek B, Heldal M, Hohloser SH, Kolh P, Le Heuzey JY, Ponikowski P, Rutten FH. Guidelines for the management of atrial fibrillation: The task force for the management of atrial fibrillation of the european society of cardiology (esc). *European heart journal*. 2010;31:2369-2429
2. Nattel S. New ideas about atrial fibrillation 50 years on. *Nature*. 2002;415:219-226
3. Haissaguerre M, Jais P, Shah DC, Takahashi A, Hocini M, Quiniou G, Garrigue S, Le Mouroux A, Le Metayer P, Clementy J. Spontaneous initiation of atrial fibrillation by ectopic beats originating in the pulmonary veins. *The New England journal of medicine*. 1998;339:659-666
4. Jahangir A, Lee V, Friedman PA, Trusty JM, Hodge DO, Kopecky SL, Packer DL, Hammill SC, Shen WK, Gersh BJ. Long-term progression and outcomes with aging in patients with lone atrial fibrillation: A 30-year follow-up study. *Circulation*. 2007;115:3050-3056
5. Nattel S, Burstein B, Dobrev D. Atrial remodeling and atrial fibrillation: Mechanisms and implications. *Circulation. Arrhythmia and electrophysiology*. 2008;1:62-73
6. de Vos CB, Pisters R, Nieuwlaat R, Prins MH, Tieleman RG, Coelen RJ, van den Heijkant AC, Allessie MA, Crijns HJ. Progression from paroxysmal to persistent atrial fibrillation clinical correlates and prognosis. *Journal of the American College of Cardiology*. 2010;55:725-731
7. Wakili R, Voigt N, Kaab S, Dobrev D, Nattel S. Recent advances in the molecular pathophysiology of atrial fibrillation. *The Journal of clinical investigation*. 2011;121:2955-2968
8. Allessie MA, Boyden PA, Camm AJ, Kleber AG, Lab MJ, Legato MJ, Rosen MR, Schwartz PJ, Spooner PM, Van Wagoner DR, Waldo AL. Pathophysiology and prevention of atrial fibrillation. *Circulation*. 2001;103:769-777
9. Schotten U, Verheule S, Kirchhof P, Goette A. Pathophysiological mechanisms of atrial fibrillation: A translational appraisal. *Physiological reviews*. 2011;91:265-325
10. Burstein B, Nattel S. Atrial fibrosis: Mechanisms and clinical relevance in atrial fibrillation. *Journal of the American College of Cardiology*. 2008;51:802-809
11. Burstein B, Comtois P, Michael G, Nishida K, Villeneuve L, Yeh YH, Nattel S. Changes in connexin expression and the atrial fibrillation substrate in congestive heart failure. *Circulation research*. 2009;105:1213-1222
12. Yue L, Xie J, Nattel S. Molecular determinants of cardiac fibroblast electrical function and therapeutic implications for atrial fibrillation. *Cardiovascular research*. 2011;89:744-753
13. Burstein B, Qi XY, Yeh YH, Calderone A, Nattel S. Atrial cardiomyocyte tachycardia alters cardiac fibroblast function: A novel consideration in atrial remodeling. *Cardiovascular research*. 2007;76:442-452
14. Kneller J, Zou R, Vigmond EJ, Wang Z, Leon LJ, Nattel S. Cholinergic atrial fibrillation in a computer model of a two-dimensional sheet of canine atrial cells with realistic ionic properties. *Circulation research*. 2002;90:E73-87
15. Dobrev D, Voigt N, Wehrens XH. The ryanodine receptor channel as a molecular motif in atrial fibrillation: Pathophysiological and therapeutic implications. *Cardiovascular research*. 2011;89:734-743
16. Gould PA, Yii M, McLean C, Finch S, Marshall T, Lambert GW, Kaye DM. Evidence for increased atrial sympathetic innervation in persistent human atrial fibrillation. *Pacing and clinical electrophysiology : PACE*. 2006;29:821-829
17. de Groot NM, Houben RP, Smeets JL, Boersma E, Schotten U, Schalij MJ, Crijns H, Allessie MA. Electropathological substrate of longstanding persistent atrial fibrillation in patients with structural heart disease: Epicardial breakthrough. *Circulation*. 2010;122:1674-1682
18. Jais P, Haissaguerre M, Shah DC, Chouairi S, Gencel L, Hocini M, Clementy J. A focal source of atrial fibrillation treated by discrete radiofrequency ablation. *Circulation*. 1997;95:572-576

19. Calkins H, Kuck KH, Cappato R, Brugada J, Camm AJ, Chen SA, Crijns HJ, Damiano RJ, Jr., Davies DW, DiMarco J, Edgerton J, Ellenbogen K, Ezekowitz MD, Haines DE, Haissaguerre M, Hindricks G, Iesaka Y, Jackman W, Jalife J, Jais P, Kalman J, Keane D, Kim YH, Kirchhof P, Klein G, Kottkamp H, Kumagai K, Lindsay BD, Mansour M, Marchlinski FE, McCarthy PM, Mont JL, Morady F, Nademanee K, Nakagawa H, Natale A, Nattel S, Packer DL, Pappone C, Prystowsky E, Raviele A, Reddy V, Ruskin JN, Shemin RJ, Tsao HM, Wilber D, Heart Rhythm Society Task Force on C, Surgical Ablation of Atrial F. 2012 hrs/ehra/ecas expert consensus statement on catheter and surgical ablation of atrial fibrillation: Recommendations for patient selection, procedural techniques, patient management and follow-up, definitions, endpoints, and research trial design: A report of the heart rhythm society (hrs) task force on catheter and surgical ablation of atrial fibrillation. Developed in partnership with the european heart rhythm association (ehra), a registered branch of the european society of cardiology (esc) and the european cardiac arrhythmia society (ecas); and in collaboration with the american college of cardiology (acc), american heart association (aha), the asia pacific heart rhythm society (aphrs), and the society of thoracic surgeons (sts). Endorsed by the governing bodies of the american college of cardiology foundation, the american heart association, the european cardiac arrhythmia society, the european heart rhythm association, the society of thoracic surgeons, the asia pacific heart rhythm society, and the heart rhythm society. *Heart rhythm : the official journal of the Heart Rhythm Society*. 2012;9:632-696 e621
20. Pappone C, Oreto G, Lamberti F, Vicedomini G, Loricchio ML, Shpun S, Rillo M, Calabro MP, Conversano A, Ben-Haim SA, Cappato R, Chierchia S. Catheter ablation of paroxysmal atrial fibrillation using a 3d mapping system. *Circulation*. 1999;100:1203-1208
21. Lin D, Frankel DS, Zado ES, Gerstenfeld E, Dixit S, Callans DJ, Riley M, Hutchinson M, Garcia F, Bala R, Verdino R, Cooper J, Marchlinski FE. Pulmonary vein antral isolation and nonpulmonary vein trigger ablation without additional substrate modification for treating longstanding persistent atrial fibrillation. *Journal of cardiovascular electrophysiology*. 2012;23:806-813
22. Parkash R, Tang AS, Sapp JL, Wells G. Approach to the catheter ablation technique of paroxysmal and persistent atrial fibrillation: A meta-analysis of the randomized controlled trials. *Journal of cardiovascular electrophysiology*. 2011;22:729-738
23. Assasi N, Xie F, Blackhouse G, Gaebel K, Robertson D, Hopkins R, Healey JS, Goeree R. Comparative effectiveness of catheter ablation strategies for rhythm control in patients with atrial fibrillation: A meta-analysis. *Journal of interventional cardiac electrophysiology : an international journal of arrhythmias and pacing*. 2012;35:259-275
24. Thomas SP, Sanders P. Catheter ablation for atrial fibrillation. *Heart, lung & circulation*.21:395-401
25. Andrade JG, Khairy P, Guerra PG, Deyell MW, Rivard L, Macle L, Thibault B, Talajic M, Roy D, Dubuc M. Efficacy and safety of cryoballoon ablation for atrial fibrillation: A systematic review of published studies. *Heart Rhythm*.8:1444-1451
26. Gerstenfeld EP. New technologies for catheter ablation of atrial fibrillation. *Current treatment options in cardiovascular medicine*.13:393-401
27. Callans DJ, Gerstenfeld EP, Dixit S, Zado E, Vanderhoff M, Ren JF, Marchlinski FE. Efficacy of repeat pulmonary vein isolation procedures in patients with recurrent atrial fibrillation. *Journal of cardiovascular electrophysiology*. 2004;15:1050-1055
28. Ouyang F, Tilz R, Chun J, Schmidt B, Wissner E, Zerm T, Neven K, Kokturk B, Konstantinidou M, Metzner A, Fuernkranz A, Kuck KH. Long-term results of catheter ablation in paroxysmal atrial fibrillation: Lessons from a 5-year follow-up. *Circulation*.122:2368-2377
29. Katritsis D, Merchant FM, Mela T, Singh JP, Heist EK, Armoundas AA. Catheter ablation of atrial fibrillation the search for substrate-driven end points. *Journal of the American College of Cardiology*.55:2293-2298
30. Oral H, Knight BP, Tada H, Ozaydin M, Chugh A, Hassan S, Scharf C, Lai SW, Greenstein R, Pelosi F, Jr., Strickberger SA, Morady F. Pulmonary vein isolation for paroxysmal and persistent atrial fibrillation. *Circulation*. 2002;105:1077-1081
31. Brooks AG, Stiles MK, Laborderie J, Lau DH, Kuklik P, Shipp NJ, Hsu LF, Sanders P. Outcomes of longstanding persistent atrial fibrillation ablation: A systematic review. *Heart Rhythm*.7:835-846

32. Rostock T, Drewitz I, Steven D, Hoffmann BA, Salukhe TV, Bock K, Servatius H, Aydin MA, Meinertz T, Willems S. Characterization, mapping, and catheter ablation of recurrent atrial tachycardias after stepwise ablation of long-lasting persistent atrial fibrillation. *Circ Arrhythm Electrophysiol*.3:160-169
33. Shen J, Bailey M, Damiano RJ, Jr. Surgery for lone atrial fibrillation: Present state-of-the-art. *Innovations (Philadelphia, Pa*. 2009;4:248-255
34. Jais P, Hocini M, O'Neill MD, Klein GJ, Knecht S, Sheiiro M, Arentes L, Kodali S, Clementy J, Haissaguerre M. How to perform linear lesions. *Heart Rhythm*. 2007;4:803-809
35. Nademanee K, McKenzie J, Kosar E, Schwab M, Sunsaneewitayakul B, Vasavakul T, Khunnawat C, Ngarmukos T. A new approach for catheter ablation of atrial fibrillation: Mapping of the electrophysiologic substrate. *Journal of the American College of Cardiology*. 2004;43:2044-2053
36. Oral H, Chugh A, Good E, Wimmer A, Dey S, Gadeela N, Sankaran S, Crawford T, Sarrazin JF, Kuhne M, Chalfoun N, Wells D, Frederick M, Fortino J, Benloucif-Moore S, Jongnarangsin K, Pelosi F, Jr., Bogun F, Morady F. Radiofrequency catheter ablation of chronic atrial fibrillation guided by complex electrograms. *Circulation*. 2007;115:2606-2612
37. Viles-Gonzalez JF, Gomes JA, Miller MA, Dukkipati SR, Koruth JS, Eggert C, Coffey J, Reddy VY, d'Avila A. Areas with complex fractionated atrial electrograms recorded after pulmonary vein isolation represent normal voltage and conduction velocity in sinus rhythm. *Europace*.
38. Lau DH, Maesen B, Zeemering S, Verheule S, Crijns HJ, Schotten U. Stability of complex fractionated atrial electrograms: A systematic review. *Journal of cardiovascular electrophysiology*.23:980-987
39. Mandapati R, Skanes A, Chen J, Berenfeld O, Jalife J. Stable microreentrant sources as a mechanism of atrial fibrillation in the isolated sheep heart. *Circulation*. 2000;101:194-199
40. Narayan SM, Krummen DE, Rappel WJ. Clinical mapping approach to diagnose electrical rotors and focal impulse sources for human atrial fibrillation. *Journal of cardiovascular electrophysiology*.23:447-454
41. Shivkumar K, Ellenbogen KA, Hummel JD, Miller JM, Steinberg JS. Acute termination of human atrial fibrillation by identification and catheter ablation of localized rotors and sources: First multicenter experience of focal impulse and rotor modulation (firm) ablation. *Journal of cardiovascular electrophysiology*.23:1277-1285
42. Cox JL, Canavan TE, Schuessler RB, Cain ME, Lindsay BD, Stone C, Smith PK, Corr PB, Boineau JP. The surgical treatment of atrial fibrillation. Ii. Intraoperative electrophysiologic mapping and description of the electrophysiologic basis of atrial flutter and atrial fibrillation. *The Journal of thoracic and cardiovascular surgery*. 1991;101:406-426
43. McCarthy PM, Gillinov AM, Castle L, Chung M, Cosgrove D, 3rd. The cox-maze procedure: The cleveland clinic experience. *Seminars in thoracic and cardiovascular surgery*. 2000;12:25-29
44. Prasad SM, Maniar HS, Camillo CJ, Schuessler RB, Boineau JP, Sundt TM, 3rd, Cox JL, Damiano RJ, Jr. The cox maze iii procedure for atrial fibrillation: Long-term efficacy in patients undergoing lone versus concomitant procedures. *The Journal of thoracic and cardiovascular surgery*. 2003;126:1822-1828
45. Shen J, Bailey MS, Damiano RJ, Jr. The surgical treatment of atrial fibrillation. *Heart Rhythm*. 2009;6:S45-50
46. Lall SC, Melby SJ, Voeller RK, Zierer A, Bailey MS, Guthrie TJ, Moon MR, Moazami N, Lawton JS, Damiano RJ, Jr. The effect of ablation technology on surgical outcomes after the cox-maze procedure: A propensity analysis. *The Journal of thoracic and cardiovascular surgery*. 2007;133:389-396
47. La Meir M, Gelsomino S, Luca F, Pison L, Colella A, Lorusso R, Crudeli E, Gensini GF, Crijns HG, Maessen J. Minimal invasive surgery for atrial fibrillation: An updated review. *Europace*.15:170-182
48. Bugge E, Nicholson IA, Thomas SP. Comparison of bipolar and unipolar radiofrequency ablation in an in vivo experimental model. *Eur J Cardiothorac Surg*. 2005;28:76-80; discussion 80-72
49. La Meir M, Gelsomino S, Luca F, Lorusso R, Gensini GF, Pison L, Wellens F, Maessen J. Minimally invasive thoracoscopic hybrid treatment of lone atrial fibrillation: Early results of monopolar versus bipolar radiofrequency source. *Interactive cardiovascular and thoracic surgery*. 2012;14:445-450
50. Knecht S, Veenhuyzen G, O'Neill MD, Wright M, Nault I, Weerasooriya R, Miyazaki S, Sacher F, Hocini M, Jais P, Haissaguerre M. Atrial tachycardias encountered in the context of catheter ablation for atrial fibrillation part ii: Mapping and ablation. *Pacing Clin Electrophysiol*. 2009;32:528-538

51. Pison L, Dagres N, Lewalter T, Proclemer A, Marinskis G, Blomstrom-Lundqvist C. Surgical and hybrid atrial fibrillation ablation procedures. *Europace*.14:939-941
52. Gelsomino S, Van Breugel HN, Pison L, Parise O, Crijns HJ, Wellens F, Maessen JG, La Meir M. Hybrid thoracoscopic and transvenous catheter ablation of atrial fibrillation. *European journal of cardio-thoracic surgery : official journal of the European Association for Cardio-thoracic Surgery*. 2013
53. Chen SA, Hsieh MH, Tai CT, Tsai CF, Prakash VS, Yu WC, Hsu TL, Ding YA, Chang MS. Initiation of atrial fibrillation by ectopic beats originating from the pulmonary veins: Electrophysiological characteristics, pharmacological responses, and effects of radiofrequency ablation. *Circulation*. 1999;100:1879-1886
54. Sakamoto S, Schuessler RB, Lee AM, Aziz A, Lall SC, Damiano RJ, Jr. Vagal denervation and reinnervation after ablation of ganglionated plexi. *The Journal of thoracic and cardiovascular surgery*.139:444-452
55. Blackshear JL, Odell JA. Appendage obliteration to reduce stroke in cardiac surgical patients with atrial fibrillation. *The Annals of thoracic surgery*. 1996;61:755-759
56. Di Biase L, Burkhardt JD, Mohanty P, Sanchez J, Mohanty S, Horton R, Gallinghouse GJ, Bailey SM, Zagrodzky JD, Santangeli P, Hao S, Hongo R, Beheiry S, Themistoclakis S, Bonso A, Rossillo A, Corrado A, Raviele A, Al-Ahmad A, Wang P, Cummings JE, Schweikert RA, Pelargonio G, Dello Russo A, Casella M, Santarelli P, Lewis WR, Natale A. Left atrial appendage: An underrecognized trigger site of atrial fibrillation. *Circulation*.122:109-118

Summary

The cornerstone of atrial fibrillation (AF) is electrical isolation of the pulmonary veins (PV). In patients with non-paroxysmal AF, PV isolation alone is insufficient and one needs to modify the atrial arrhythmogenic substrate. AF ablation is mostly performed using a transvenous, endocardial approach with catheters. This technique enables one to characterize the underlying substrate in order to tailor the ablation procedure but these ablation lesions are not always transmural nor long lasting. Thoracoscopic surgical AF ablation techniques, on the other hand, create more reliable linear lesions but the lesion set is based on empirical assumptions rather than specific patient characteristics. Performed in combination (hybrid AF ablation), both approaches are complementary as they overcome their mutual shortcomings. In this thesis, we demonstrated that the hybrid AF ablation procedure is safe and feasible. Medium and long-term results are encouraging, especially in currently challenging settings such as non-paroxysmal AF and failed endocardial catheter ablation procedures.

Samenvatting (Summary in Dutch)

Boezemfibrilleren (ook atriumfibrilleren of voorkamerfibrillatie genoemd) is de meest voorkomende ritmestoornis van het hart. De kans om deze ritmestoornis te ontwikkelen is groter dan 20% bij 55-plussers. De handtekening van boezemfibrilleren is de abnormale elektrische activiteit ter hoogte van de atria van het hart (ook voorkamers of boezems genoemd). Deze abnormale elektrische activiteit, resulteert in een verminderde pompwerking van de atria en een snelle en onregelmatige pols. Naast klachten van o.a. hartkloppingen, is er een grotere kans op het ontwikkelen van bloedklonters in het hart. Patiënten met boezemfibrilleren hebben hierdoor een duidelijk verhoogd risico op het ontwikkelen van een beroerte.

De behandeling van boezemfibrilleren concentreert zich op het voorkomen van bloedklonters en het controleren (vertragen) of normaliseren van het hartritme. Het herstellen van het normale en regelmatig hartritme kan gebeuren middels medicijnen of bepaalde ingrepen (ablatie). Het voordeel van een ablatie is de mogelijkheid om zonder medicijnen vrij te zijn van deze ritmestoornis.

Tijdens zo'n ablatie worden littekens gemaakt ter hoogte van de atria. Deze littekens fungeren als een 'electrische barrière': ze houden de abnormale prikkels tegen die aanleiding kunnen geven tot het boezemfibrilleren. Een fundamentele voorwaarde hierbij is dat het litteken doorheen de volledige dikte van het weefsel reikt (men spreekt van transmuraliteit).

Er bestaan tegenwoordig twee manieren om deze littekens te maken. De eerste is de zogenaamde percutane benadering: via de lies gaat de electrofysioloog draadjes (catheters) opvoeren tot in het hart en middels warmte, koude of laser worden de littekens gecreëerd. Het grote voordeel van deze benadering is de mogelijkheid om precies te bepalen waar in de atria precies bepaalde littekens dienen gemaakt te worden om een maximaal effect te bekomen. Het grote nadeel echter, is de veelal beperkte 'kwaliteit' van deze littekens: mettertijd kunnen deze meer en meer abnormale elektrische prikkels doorlaten (**Hoofdstuk 2**). Een belangrijke reden hiervoor is dat dergelijke littekens niet steeds volledig transmuraal zijn. Een tweede manier om littekens te maken is de thoracoscopische benadering. Hierbij gaat de hartchirurg via een kijkoperatie littekens maken aan de buitenkant van de atria. Littekens die op een dergelijke manier worden gemaakt zijn bijna steeds volledig transmuraal en derhalve bijzonder effectief in het tegenhouden van abnormale elektrische prikkels. Het probleem waar de chirurg mee geconfronteerd wordt, is dat hij niet de middelen heeft om te bepalen welke littekens in een bepaalde patiënt dienen gemaakt om zoveel mogelijk het boezemfibrilleren te voorkomen (**Hoofdstuk 3**).

Theoretisch lijken beide benaderingen complementair te zijn: efficiënte littekens (gemaakt door de chirurg) worden op de juiste plaats ter hoogte van de atria (bepaald door de electrofysioloog) gecreëerd hetgeen resulteert in het voorkomen van boezemfibrilleren.

Daarom hebben we een procedure ontwikkeld waarbij de percutane en thoracoscopische benadering simultaan worden toegepast bij patiënten met boezemfibrilleren. Bij een dergelijke hybride ablatie gaat de cardiochirurg een aantal littekens maken op de atria via de thoracoscopische benadering. Tijdens dezelfde ingreep gaat de electrofysioloog aan de binnenkant van de atria de transmuraliteit van deze littekens evalueren. Littekens die niet volledig transmuraal zijn, kunnen door de electrofysioloog aangevuld worden. Deze laatste kan ook onderzoeken of er eventueel bijkomende littekens dienen gemaakt om het boezemfibrilleren tegen te houden.

Dit proefschrift onderzoekt de haalbaarheid en veiligheid van een dergelijke hybride ingreep (**Hoofdstuk 4-6**). In **hoofdstuk 7 en 8** beschrijven we twee observaties die het nut van de hybride ablatie onderstrepen. De lange termijn resultaten van de hybride ingreep worden beschreven in **hoofdstuk 9**.

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Gepassioneerd, gefascineerd voor mijn vak, gepassioneerd, gefascineerd voor mijn naasten.

Professor Mullens, beste Wilfried
My best man. Op belangrijke officiële aangelegenheden in mijn leven, was en ben je steeds mijn getuige. Ik zou nu niet anders willen. Sinds onze assistentenjaar in Genk is mijn waardering voor jou een statement. Samen met Nele betekent jullie vriendschap bijzonder veel voor ons. Stralend in zijn eenvoud. Kwaliteit boven kwantiteit.

Professor La Meir, beste Mark,
Voici mon ami! Het is beter een mijl te reizen dan duizend boeken te lezen. Confucius had gelijk. Onze trip naar China was er eentje van banden smeden. Vruchtbaar en intens. “Dju La Meir”, ik weet dan dat het niet goed zit. Superlatieven. Mon ami, merci pour tout!

De klok tikt onverminderd verder en mijn verhaal geeft me een emotioneel gevoel. Ieder op zich betekent zoveel voor me. Gehuld in de stilte van de nacht nadenken over wie je zo dankbaar bent. Je komt jezelf tegen. Je beseft dat je bent wie je bent door de mensen rondom jou.

Rondom me. Dankbaarheid voor een pot zelfgemaakte choco of een stuk chocolade van moe en ma. Tantes en nichtjes die ‘via via’ vragen hoe het gaat. Ochtendlijke koffieklets bij oma, wekelijkse kapsalon bij oma, iedereen toonde zijn interesse. Collega’s van Cindyke, ik ben vervuld met warmte. Jos en Miel, het is iedere keer een waar plezier om met jullie te gaan fietsen. Nonkel Roland, door te luisteren naar mijn electrofysiologisch verhaal heb jij in beeld gebracht wat ik denk en voel.

Carole & Alain,
Salomé, Néomie, Caïn, Anthony & Matisse,
Zusje, ik denk terug aan de tijd dat we samen examens hadden. Nu zoveel jaren later hebben we ieder ons drukke leven met beide onze carrière en gezin. Ik denk terug aan

de telefoon dat je na een ongeval opgenomen was op spoed. Hoe druk ook, ik wou bij je zijn, mijn zus.

09/03 Charlot, 18/04 Seth, 16/05 Baue, 01/07 Salomé, 24/10 Feliz: jullie verjaardagen staan op de kalender van jullie peteke en peter Laurent met stip genoteerd!

Tom & Heidi,
Baue & Feliz,
Waar begin ik? Heb je enkele pagina's de tijd? Ik kan een boek vol herinneringen schrijven. Tom, ik mocht van je talenten proeven als regisseur toen je onze hybride ingreep monteerde. De beelden waren wat van het goede teveel, maar voor mij beet je door. De zaterdagen bij oma aan tafel zijn legendarisch. Geen enkele tv-serie of film kan hieraan tippen. Ik kijk naar je op. Je creatief talent, je levensprincipes. Heerlijk om met jou te praten.
Heidi, zoals ik op de speech tijdens jullie huwelijk al kwam te zeggen, hebben we een speciale band. De 'niet-Willems-band'. Ze spreken een taal die we niet verstaan, humor die we amper kunnen vatten. Maar naast het gezellige clan-gebeuren zie je wie we zijn. Waar wij het soms ook moeilijk hebben. Je steunde me de laatste dagen en weken continu. Net zoals je er voor Cindyke continu bent. Een korte sms, een lange sms, een telefoontje. Je bent een lieve schoonzus.

Kerstmis is voor ons een bijzondere tijd. We genieten van jullie op kerstavond.

Annie & René,
weinig woorden zeggen soms meer dan vele zinnen. René jij weet als geen ander wat ik zonder woorden bedoel. Jullie behandelen me als jullie eigen zoon. Taxi-René is een begrip geworden en de zaterdagen bij jullie aan tafel zijn als een wekelijkse Sinterklaasavond. Bedankt voor al die keren dat je het gras hebt gedaan. Annie = mitten im Paradies! De sfeer en gezelligheid die ik bij jullie heb gevonden zijn niet te evenaren.
Maman et Pierre,
Ma maman, qui m'a fait comprendre que la vie n'est pas faite que de problèmes qu'on pourrait résoudre grâce à des formules mathématiques et des algorithmes. Maintenant j'espère que papa est fier de moi… Mais grâce à Pierre j'ai eu la chance d'avoir un deuxième père !
Cher maman, cher Pierre,
votre intelligence, votre confiance, et votre amour me portent et me guident tous les jours. La distance entre Koersel et Bretagne est énorme. Mais chaque téléphone, message m'a fait beaucoup de plaisirs!

Jongens van mij!

Oplaaien, de zee, ‘ik kan niet binnen’, DiPi kamp, de titel is de kip… ik herinner het mij allemaal alsof het gisteren was.

Gertjan, van Stal via Geel naar Lommel en zo tot… Je wordt groot, man! Weet je dat ik iedere dag nog leer van jou? Je doorzettingsvermogen zijn mijn drijfveer. Je stuurt me dan een smsje: je bent een beest, papa, je kan dat! Het heeft lang geduurd vooraleer ik door had wat een beest betekende. Maar het is een compliment. Ik ben zo trots op je, jongen. Jij bent mijn beest!

Emile, gekke Emile, je bent zo heerlijk, zo creatief! Terwijl ik zat te schrijven kom jij met je muziek voor me staan dansen! Emile gij zijt niet normaal! Maar zo prachtig! Jullie mij maar uitlachen met de ‘hybride oke’! Jij weet iets waar anderen een heel leven naar zoeken (en vaak niet vinden): jij bent gelukkig met wat je hebt en niet ongelukkig om hetgeen je niet hebt…

Jules, zelfs wetenschap is geen zekerheid... In de zak van mijn jas stop je steeds je sleutelhanger van Sint-Christoffel. De beschermheilige van de reizigers. Ik draag hem steeds met me mee. Je gedachten en gevoelens hebben geen grenzen. Terwijl ik dit schrijf betrap ik mezelf… Weet je het nog van je eigendomsakte? Niet te volgen! Blijf voor altijd zoals je bent en geloof in jezelf!

Lieve jongens van me, ik waak over jullie.

Het is midden in de nacht nu. Mijn cirkel is gesloten. Ik ben rond.

Mijn allerliefste, mijn Cindyke,
Geen woorden voor jou. Het eerste en meest oprechte wat in mij opkomt is een liedje waar jij en ik zo graag naar luisteren: “I say a little prayer for you…”. Ik sluit af, check even de jongens. Ik kom nu naar je toe en kruip dicht tegen je aan. Ik hoop zo dat je rustig slaapt.

Hora est

Curriculum vitae

Laurent Pison was born on the 16th of October 1973 in Leuven, Belgium. After completing secondary school at Sint Albertus College in Haasrode in 1992, he started his medical training at the Katholieke Universiteit Leuven and obtained his medical degree in 1999. He finished his cardiology training in 2005 and started working as an Electrophysiology Fellow under supervision of prof. dr. H. Heidbüchel at the Department of Cardiology of UZ Gasthuisberg Leuven. In 2007, he started as cardiologist-electrophysiologist and staff member at the Department of Cardiology of Maastricht University Medical Center. His research activities are mainly focused on atrial fibrillation. He presented his work at multiple national and international medical congresses, and acts as reviewer for several international journals. He is member of the Scientific Initiatives Committee of the European Heart Rhythm Association.

Publications

- **Pison L**, Proclemer A, Bongiorni MG, Marinskis G, Hernandez-Madrid A, Blomström-Lundqvist C; Scientific Initiative Committee, European Heart Rhythm Association. Imaging techniques in electrophysiology and implantable device procedures: results of the European Heart Rhythm Association survey. Europace. 2013 Sep;15(9):1333-6.

- Gelsomino S, Van Breugel HN, **Pison L**, Parise O, Crijns HJ, Wellens F, Maessen JG, La Meir M. Hybrid thoracoscopic and transvenous catheter ablation of atrial fibrillation. Eur J Cardiothorac Surg. 2013 Jul 31.

- Proclemer A, Lewalter T, Bongiorni MG, Nielsen JH, **Pison L**, Lundqvist CB; conducted by the Scientific Initiative Committee, European Heart Rhythm Association. Screening and risk evaluation for sudden cardiac death in ischaemic and non-ischaemic cardiomyopathy: results of the European Heart Rhythm Association survey. Europace. 2013 Jul;15(7):1059-62.

- Dagres N, Lewalter T, Lip GY, **Pison L**, Proclemer A, Blomström-Lundqvist C; Scientific Initiatives Committee, European Heart Rhythm Association. Current practice of antiarrhythmic drug therapy for prevention of atrial fibrillation in Europe: The European Heart Rhythm Association survey. Europace. 2013 Apr;15(4):478-81.

- Marinskis G, Bongiorni MG, Dagres N, Lewalter T, **Pison L**, Blomstrom-Lundqvist C; Scientific Initiative Committee, European Heart Rhythm Association. X-ray exposure hazards for physicians performing ablation procedures and device implantation: results of the European Heart Rhythm Association survey. Europace. 2013 Mar;15(3):444-6

- Proclemer A, Dagres N, Marinskis G, **Pison L**, Lip GY, Blomstrom-Lundqvist C; Scientific Initiative Committee, European Heart Rhythm Association. Current practice in Europe: how do we manage patients with ventricular tachycardia? European Heart Rhythm Association Survey. Europace. 2013 Feb;15(2):167-9.

- Lip GY, Dagres N, Proclemer A, Svendsen JH, **Pison L**, Blomstrom-Lundqvist C; Scientific Initiative Committee, European Heart Rhythm Association. Left atrial appendage occlusion for stroke prevention in atrial fibrillation in Europe: results of the European Heart Rhythm Association survey. Europace. 2013 Jan;15(1):141-3.

- Lewalter T, Dobreanu D, Proclemer A, Marinskis G, **Pison L**, Blomström-Lundqvist C; conducted by the Scientific Initiative Committee, European Heart Rhythm Association. Atrial fibrillation ablation techniques. Europace. 2012 Oct;14(10):1515-7.

- Weijs B, Pisters R, Haest RJ, Kragten JA, Joosen IA, Versteylen M, Timmermans CC, **Pison L**, Blaauw Y, Hofstra L, Nieuwlaat R, Wildberger J, Crijns HJ. Patients originally diagnosed with idiopathic atrial fibrillation more often suffer from insidious coronary artery disease compared to healthy sinus rhythm controls. Heart Rhythm. 2012 Dec;9(12):1923-9.

- Proclemer A, Dobreanu D, **Pison L**, Lip GY, Svendsen JH, Lundqvist CB; Scientific Initiative Committee-European Heart Rhythm Association. Current practice in out-of-hospital cardiac arrest management: a European Heart Rhythm Association EP network survey. Europace. 2012 Aug;14(8):1195-8.

- La Meir M, Gelsomino S, Lorusso R, Lucà F, **Pison L**, Parise O, Wellens F, Gensini GF, Maessen J. The hybrid approach for the surgical treatment of lone atrial fibrillation: One-year results employing a monopolar radiofrequency source. J Cardiothorac Surg. 2012 Jul 19;7:71.

- La Meir M, Gelsomino S, Lucà F, **Pison L**, Colella A, Lorusso R, Crudeli E, Franco Gensini G, Crijns HG, Maessen J. Minimal invasive surgery for atrial fibrillation: an updated review. Europace. 2013 Feb;15(2):170-82.

- **Pison L**, La Meir M, van Opstal J, Blaauw Y, Maessen J, Crijns HJ. Hybrid thoracoscopic surgical and transvenous catheter ablation of atrial fibrillation. J Am Coll Cardiol. 2012 Jul 3;60(1):54-61.

- **Pison L**, Dagres N, Lewalter T, Proclemer A, Marinskis G, Blomström-Lundqvist C; Scientific Initiative Committee, European Heart Rhythm Association. Surgical and hybrid atrial fibrillation ablation procedures. Europace. 2012 Jul;14(7):939-41.

- La Meir M, Gelsomino S, Lucà F, **Pison L**, Rao CM, Wellens F, Maessen JG. Improvement of left atrial function and left atrial reverse remodeling after minimally invasive radiofrequency ablation evaluated by two-dimensional speckle tracking echocardiography. J Thorac Cardiovasc Surg. 2013 Jul;146(1):72-7.

- Bongiorni MG, Blomström-Lundqvist C, Kennergren C, Dagres N, **Pison L**, Svendsen JH, Auricchio A; Scientific Initiative Committee, European Heart Rhythm Association. Current practice in transvenous lead extraction: a European Heart Rhythm Association EP Network Survey. Europace. 2012 Jun;14(6):783-6.

- La Meir M, Gelsomino S, Lucà F, **Pison L**, Parise O, Colella A, Gensini GF, Crijns H, Wellens F, Maessen JG. Minimally invasive surgical treatment of lone atrial fibrillation: Early results of hybrid versus standard minimally invasive approach employing radiofrequency sources. Int J Cardiol. 2013 Aug 20;167(4):1469-75.

- Hendriks JM, de Wit R, Crijns HJ, Vrijhoef HJ, Prins MH, Pisters R, **Pison L**, Blaauw Y, Tieleman RG. Nurse-led care vs. usual care for patients with atrial fibrillation: results of a randomized trial of integrated chronic care vs. routine clinical care in ambulatory patients with atrial fibrillation. Eur Heart J. 2012 Nov;33(21):2692-9.

- Marinskis G, van Erven L, Bongiorni MG, Lip GY, **Pison L**, Blomström-Lundqvist C; Scientific Initiative Committee, European Heart Rhythm Association. Practices of cardiac implantable electronic device follow-up: results of the European Heart Rhythm Association survey. Europace. 2012 Mar;14(3):423-5.

- La Meir M, Gelsomino S, Lucà F, Lorusso R, Gensini GF, **Pison L**, Wellens F, Maessen J. Minimally invasive thoracoscopic hybrid treatment of lone atrial fibrillation: early results of monopolar versus bipolar radiofrequency source. Interact Cardiovasc Thorac Surg. 2012 Apr;14(4):445-50.

- **Pison L**, La Meir M, Crijns HJ. Left atrial flutter due to incomplete left fibrous trigone linear lesion. J Thorac Cardiovasc Surg. 2011 Nov;142(5):e149-51.

- La Meir M, Gelsomino S, Luca F, **Pison L**, Chambille P, Parise O, Crijns HJ, Maessen JG. Time-related prevalence of postoperative atrial fibrillation after stand-alone minimally invasive radiofrequency ablation. J Card Surg. 2011 Jul;26(4):453-9.

- Weijs B, Blaauw Y, Rennenberg RJ, Schurgers LJ, Timmermans CC, **Pison L**, Nieuwlaat R, Hofstra L, Kroon AA, Wildberger J, Crijns HJ. Patients using vitamin K antagonists show increased levels of coronary calcification: an observational study in low-risk atrial fibrillation patients. Eur Heart J. 2011 Oct;32(20):2555-62.

- van Opstal JM, Blaauw Y, **Pison L**. A completely subcutaneous implantable cardioverter defibrillator in a patient with situs inversus totalis. J Cardiovasc Electrophysiol. 2012 Mar;23(3):333.

- **Pison L**, La Meir M, van Opstal J, Crijns HJ. Transient clamp-induced mechanical block of pulmonary vein potentials. J Thorac Cardiovasc Surg. 2011 Feb;141(2):e15-6.

- Blaauw Y, **Pison L**, van Opstal JM, Dennert RM, Heesen WF, Crijns HJ. Reversal of ventricular premature beat induced cardiomyopathy by radiofrequency catheter ablation. Neth Heart J. 2010 Oct;18(10):493-8.

- **Pison L**, Timmermans C, Rodriguez LM. Cryoablation of a left coronary cusp ventricular tachycardia. Heart. 2010 Nov;96(22):1862.

- van Opstal JM, Timmermans C, Blaauw Y, **Pison L**. Bronchial erosion and hemoptysis after pulmonary vein isolation by cryoballoon ablation. Heart Rhythm. 2011;8(9):1459.

- **Pison L**, LA Meir M, Maessen J, Crijns H. Seeing is Believing: Unmasking Left Atrial Appendage Activity Recorded in the Left Superior Pulmonary Vein Without Stimulation. J Cardiovasc Electrophysiol. 2010 Jun 25.

- **Pison L**, La Meir M, Maessen J, Crijns H. Extracardiac ice formation during cryoballoon technique for atrial fibrillation. Heart Rhythm. 2010 Oct;7(10):1518.

- De Vos CB, **Pison L**, Pisters R, Schotten U, Cheriex EC, Prins MH, Delhaas T, Crijns HJ, Tieleman RG. Atrial fibrillatory wall motion and degree of atrial remodeling in patients with atrial fibrillation: a tissue velocity imaging study. J Cardiovasc Electrophysiol. 2009 Dec;20(12):1374-81.

- Sauren LD, la Meir M, de Roy L, **Pison L**, van der Veen FH, Mess WH, Crijns HJ, Maessen JG. Increased number of cerebral emboli during percutaneous endocardial pulmonary vein isolation versus a thoracoscopic epicardial approach. Eur J Cardiothorac Surg. 2009 Nov;36(5):833-7.

- Sauren LD, VAN Belle Y, DE Roy L, **Pison L**, LA Meir M, VAN DER Veen FH, Crijns HJ, Jordaens L, Mess WH, Maessen JG. Transcranial measurement of cerebral microembolic signals during endocardial pulmonary vein isolation: comparison of three different ablation techniques. J Cardiovasc Electrophysiol. 2009 Oct;20(10):1102-7.

- Manusama R, Timmermans C, **Pison L**, Philippens S, Perez D, Rodriguez LM. Typical atrial flutter can effectively be treated using single one-minute cryoapplications: results from a repeat electrophysiological study. J Interv Card Electrophysiol. 2009 Oct;26(1):65-72.

- Ector J, Ganame J, van der Merwe N, Adriaenssens B, **Pison L**, Willems R, Gewillig M, Heidbüchel H. Reduced right ventricular ejection fraction in endurance athletes presenting with ventricular arrhythmias: a quantitative angiographic assessment. Eur Heart J. 2007 Feb;28(3):345-53.

- Mullens W, **Pison L**, Vandervoort P, Eerdekens J, De Vusser P. Multiple exercise induced syncopal episodes in a young woman due to arrhythmogenic right ventricular dysplasia. Europace. 2005 Mar;7(2):154-7.

- **Pison L**, De Vusser P, Mullens W. Apical ballooning in relatives. Heart. 2004 Dec;90(12):e67.

- Corluy L, **Pison L**, Lauweryns P, Samson I, Westhovens R. An unusual non-traumatic atlantoaxial subluxation in an adult patient: Grisel's syndrome.Clin Rheumatol. 2004 Apr;23(2):182-3.

Abstracts and Posters

- **Laurent Pison**, Marc La Meir, Jos Maessen, and Harry Crijns. Hybrid thoracoscopic surgical and transvenous catheter ablation of AF, towards single procedure ablation of longstanding AF. Heart Rhythm Society 2010
- **Laurent Pison**, Pim Peeters, Yuri Blaauw, Suzanne Philippens, Harry J. Crijns, Johan Vlaeyen,
Jean Schoenen, Carl Timmermans. Most Patients have Headache during Balloon Cryo-ablation for Atrial Fibrillation. American Heart Association Scientific Sessions, Orlando - Florida, 2011
- **Laurent Pison**, Jurren van Opstal, Yuri Blaauw, Suzanne Philippens, Harry Crijns, Carl Timmermans. Point-by-point versus balloon cryoablation in patients with paroxysmal atrial fibrillation. ECAS, Paris - France, 2011
- **Laurent Pison**, Pim Peeters, Yuri Blaauw, Kevin Vernooy, Suzanne Philippens, Harry J. Crijns, Johan Vlaeyen, Jean Schoenen, Carl Timmermans. Majority of AF patients feels headache during cryoballoon ablation. ECAS, Paris - France, 2013.

Presentations

- **Laurent Pison**. EP/Surgeon Collaboration: New Frontiers in Cardiac Ablation. Satellite meeting during Boston AF Symposium Annual Meeting, 2009.
- **Laurent Pison.** A hybrid thoracoscopic ablation with endocardial EP endpoints. Latest updates in the surgical treatment of AF, Vienna - Austria, 2009.
- **Laurent Pison**. AF: from cellular electrophysiology to hybrid strategies for ablation. ISMICS 2010.
- **Laurent Pison.** Hybrid ablation for atrial fibrillation and LAA closure. ALMA meeting, Maastricht - Netherlands, 2010.
- **Laurent Pison**. Ablation of AF. CREATE Minicourse, Maastricht - Netherlands, 2009.
- **Laurent Pison.** Preliminary results of the tailored hybrid approach. European Cardiac Course, Maastricht - Netherlands, 2010.
- **Laurent Pison**, Mark La Meir, Jos Maessen, Harry J. Crijns. Management of recurrent atrial arrhythmias after hybrid thoracoscopic surgical and transvenous catheter ablation of atrial fibrillation. Venice Arrhythmias 2011
- **Laurent Pison.** Hybrid AF ablation. Ziekenhuis Oost Limburg, Genk - Belgium, 2012.
- **Laurent Pison.** Results of the Maastricht endo-epicardial hybrid ablation. Hybrid AF Ablation – Crossing borders in AF ablation. Maastricht - Netherlands, 2012.

- **Laurent Pison.** Hybrid AF ablation. Satellite meeting during Boston AF Symposium Annual Meeting, 2013
- **Laurent Pison**. Hybride AF ablatie MUMC – Resultaten en indicaties. Catheterablatie van supraventriculaire en ventriculaire aritmieën, Thorn - Netherlands, 2013
- **Laurent Pison**. What is the ideal hybrid approach – an EP. 2013 ISMICS Annual Meeting *Masters Class: AFib*.
- **Laurent Pison.** EP Wire – Surgical and hybrid AF ablation procedures. Europace, Athens - Greece, 2013.
- **Laurent Pison.** Safety and feasibility of adenosine administration during hybrid atrial fibrillation ablation to test dormant pulmonary vein conduction. 18th World Congress on Heart Disease, Vancouver - Canada, 2013.
- **Laurent Pison.** XXV Giornate cardiologiche Torinesi – Advances in Cardiac Arrhythmias and Great Innovations in Cardiology, Turin - Italy, 2013.